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The British quarterly scientific journal ENDEAVOUR was first published, by Imperial Chemical Industries Limited, in January 1942. Its purpose is to provide scientists, especially those overseas, with news of the progress of the sciences. While emphasis is laid upon British work, occasional articles from overseas contributors are included and impartial reference is made to the world's scientific literature. To make the journal truly international in character it is published in five separate editions—English, French, German, Italian, and Spanish.

No charge is made for ENDEAVOUR. It is distributed to senior scientists, scientific institutions, and libraries throughout the world, the guiding principle being that of helping scientists overseas to maintain those contacts which their British colleagues have always so much valued. Within these limits the Editors are at all times glad to consider the addition of new names to the mailing list.

The drawing on the cover is of the bark Endeavour, *which, commanded by Captain James Cook and carrying a number of scientific workers, was sent out by the British Admiralty in* 1768 *to chart the South Pacific Ocean and observe the transit of Venus*

ENDEAVOUR

A quarterly review designed to record the progress of the sciences in the service of mankind

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The start of the International Geophysical Year

The great enterprise known as the International Geophysical Year—in which 56 nations are co-operating—has been planned as a concerted attack on many problems relating to the various earth sciences, for whose solution concurrent observations in different regions of the world are required. The planning stage has now been completed. The operational stage formally commenced on 1st July, 1957, although test observations were made at most stations during the preceding weeks to ensure that all equipment was in correct adjustment and that observers were thoroughly familiar with the techniques involved.

The planning of the programme has been the responsibility of the Special Committee for the International Geophysical Year, appointed by the International Council of Scientific Unions. This Committee held a preliminary meeting in Brussels in 1953, and full meetings in Rome in 1954, in Brussels in 1955, and in Barcelona in 1956. At the last two of these meetings it met in conjunction with an Advisory Committee, composed of one representative of each nation participating in the programme. A National Committee has been set up in each participating country to formulate the national share in the general programme. Recent discussions have resulted in modifications in some details of national plans, whereby a better distribution of observing stations was secured. Regional conferences have been held to discuss matters of special importance and interest to particular regions. They have included three conferences on the Antarctic, and one each on the Arctic, the western hemisphere, Eastern Europe, and the Western Pacific.

A feature of the International Geophysical Year will be the special attention given to the Antarctic, where simultaneous observations of geophysical phenomena at a number of stations have never previously been made: in neither of the two International Polar Years (1882–3 and 1932–3) were there any stations in the Antarctic. Within the Antarctic Circle there will be 57 observing stations, manned by twelve countries. Many of the stations on the Antarctic Continent were set up during the summer of 1955–56, and observations at some of them are already in progress. For communication between stations in the Antarctic, and between them and the outside world, a complete network of radio communications has been arranged. Call-signs have been allotted for each of the fixed stations and for many others operating from sledges, tracked vehicles, and aircraft. Provision has been made for direct intercommunication between all these stations, and for direct links from them to distant capital cities. Reports on meteorology, on other scientific observations, and on administrative and personal matters can thus be sent speedily and accurately. Frequencies for the various stations have been selected so as to avoid mutual interference between stations as far as possible.

The International Geophysical Year has been timed to cover a period when solar activity is at or near its maximum. Because of the various terrestrial effects resulting from disturbances on the Sun, it is important that particularly intensive observation should be made while such disturbances are in progress. But accurate prediction of the occurrence of a disturbance is not possible, though solar observations may indicate the probability that one is impending. To warn observers to be on the alert for the outburst of a disturbance, a world warning agency has been set up at Fort Belvoir, near Washington, a radio field station of the U.S. National Bureau of Standards. On the basis of information received from solar observing stations this agency will decide when to announce an alert. Should further information indicate that a disturbance is to be expected, the warning agency will declare a Special World Interval, which will start eight hours after the warning message has been given. More intensive observations in the various disciplines will then commence, and will continue until the Interval is cancelled, if the disturbance fails to materialize, or until the disturbance has subsided or the disturbed area has passed round the limb of the Sun. The warning messages will be issued at 1600 UT daily, whenever there is a state of alert or a Special World Interval, and will state whether either is to be continued or terminated.

Regional warning centres have been established in Western Europe, Eurasia, the Western Pacific, and the western hemisphere; there are also several associate centres, for example in Antarctica and Australia. The world warning agency will send a direct telegram to all regional warning centres and will also arrange for suitable signals to be

transmitted twice daily on the WWV standard-frequency broadcasts of the Bureau of Standards. Each regional warning centre will assemble summaries of current observations of geomagnetic and auroral data, of solar flares, radio fade-outs, and other phenomena, on the basis of information received, and will be responsible for distributing such information by telegrams to all stations within its region. Codes for all messages from the world and regional warning centres have been formulated.

A special feature of the observational programme will be the employment of rockets and satellite vehicles to extend observations to heights far beyond the maximum height of about 30 km that will be reached by balloons. The United States, the Soviet Union, Great Britain, and France have rocket programmes. The rockets will penetrate through the ozone layer of the atmosphere and enable the solar spectrum to be photographed into the far ultraviolet and X-ray regions. Some will carry magnetometers for the detection and measurement of the circulating current sheets whose existence has been assumed in order to account for some of the observed variations in the Earth's magnetic field. Direct measurements will be made of the ion and electron densities in and between the several ionized layers of the ionosphere. The temperature, pressure, density, and composition of the atmosphere up to great heights will be determined. It is hoped that among the rocket flights a few will occur at times when a major disturbance is taking place on the Sun.

The duration of the flight of a rocket is limited to a few minutes. The United States and the Soviet Union plan to supplement the information obtained from rocket flights by launching satellite vehicles which will circle the earth at a height of a few hundred miles and will send information back to the earth by radio. The United States has announced that it hopes to launch up to twelve artificial satellites during the course of the Year; the first of these launchings will be made in the early part of next year. The satellite, which will have a diameter between 20 and 30 in, will be launched from a three-stage rocket. It will be projected, when at a height of 200–300 miles, in a horizontal direction with a speed of 18 000 miles per hour. The orbit that it is hoped to obtain is slightly elliptical, reaching a distance of about 800 miles from the Earth at apogee. The plane of the orbit will be inclined at an angle of 40° to the equator; as the Earth rotates, the satellite, circling the globe in about 90 minutes, will pass over different regions of the Earth's surface during each revolution. Each satellite will carry complex instruments specially designed on a small scale; these are now in course of development. It will send radio signals to the Earth, where ground radar installations will be used to track its course. An elaborate organization has been arranged for securing visual and photographic observations, with provision for very accurate timing.

The resistance of the atmosphere will cause the satellite gradually to lose energy and to spiral inwards towards the Earth. As it reaches denser regions of the atmosphere it will become heated and will finally disintegrate and be vaporized, very much like a shooting star. An electronic computer will be used to compute its orbit, and it is expected that information about the density of the atmosphere at different heights will be derived. Ultraviolet and X-ray radiation from the Sun will be measured; the Earth's magnetic field above the ionosphere will be investigated; cosmic radiation will be studied by counter techniques, and, in particular, information will be obtained about the lower-energy end of the cosmic ray spectrum. Some information may be gained about micro-meteorites and about the densities of dust and of hydrogen atoms and ions in the upper atmosphere. The Soviet Union has plans to launch one or two satellites, but no information has yet been given of the nature of the orbits to be attained.

The observational data that will be accumulated during the eighteen-month programme of the International Geophysical Year will provide the basis for the investigation of a great variety of problems in geophysics. Many years must elapse before the data can be fully analysed. The important problem of how best to make the data available to geophysicists has been considered by the Special Committee. It has been decided to establish three World Data Centres—one of which will be in the United States, one in the Soviet Union, and the third in Western Europe—where copies of observations, magnetographs, ionograms, and so on will be stored. Instruction manuals have been prepared for the guidance of observers in the various disciplines in the maintenance and adjustment of equipment, in the interpretation and scaling of records, and in the uniform presentation of results.

The start of this tremendous enterprise is the culmination of years of detailed planning throughout the world. We send our good wishes for its success to all those who have made it possible and to those taking part in the observational programme.

Control of metabolic processes

H. A. KREBS

Biochemical research over the past thirty years has established that the principal metabolic processes proceed through a number of intermediate stages. What may be called the qualitative analysis of metabolic processes is now beginning to be followed by a quantitative one. This analysis seeks to elucidate the factors which determine the rates of individual metabolic processes and ensure that the complex series of biochemical changes that continuously take place in a living organism assume a pattern appropriate to its needs and environment.

Investigations into metabolic processes during the last three decades have been concerned mainly with the elucidation of the intermediary stages and with the properties of the enzymes controlling each stage. Thanks to the new tools which have become available—such as the techniques of enzymology, the use of isotopes, and chromatographic and optical methods of analysis—success has not been lacking, and the main stages of intermediary metabolism are now known. This is true for both the degradation of foodstuffs and the processes that transfer the energy derived from this degradation; it is true also for many synthetic reactions, especially those leading to the formation of constituents of low molecular weight, like fatty or amino acids.

While many details of the metabolic pathways still remain to be established, interest has recently been shifting towards other aspects of intermediary metabolism, in particular the mechanisms which govern metabolic rates [1–4]. It is well known that these are not constant, but vary with the physiological state of the cell. They may increase many times over, for example, when a tissue such as muscle or a gland changes from rest to activity. The type of metabolic process within cells may change when the environment changes. Thus energy may be obtained by oxidations if air is available, or by fermentations of sugar if it is not. It follows that cells possess mechanisms which adjust metabolic activities to changing needs.

Control of biological processes is commonly taken to be the function of hormones and of the nervous system, and there is no doubt that both play a part in some of the mechanisms which control reaction rates in higher organisms. But control mechanisms also occur in lower forms of life, such as the unicellular ones, where hormones and nerve cells are absent. These 'primitive' control mechanisms [5] are also present in higher animals; they are, in fact, the basic systems on which the action of hormones or the nervous system is superimposed.

Knowledge of intermediary metabolism and of enzyme systems has sufficiently advanced in recent years to prepare the ground for a study of these 'primitive' mechanisms which operate in controlling the rate of metabolic processes, and to give tentative answers to the question of how cells adapt the rates of some reactions to changing needs. This is particularly true of the processes supplying energy, and the following discussion will be mainly concerned with this aspect of metabolism.

The following abbreviations have been used in the formulae in this article:

ATP	adenosine triphosphate
ADP	adenosine diphosphate
ITP	inosine triphosphate
IDP	inosine diphosphate
DPN	diphosphopyridine nucleotide
$DPNH_2$	reduced diphosphopyridine nucleotide
CoA or HS-CoA	coenzyme A
P	orthophosphate

THE ROLE OF ENZYME AND SUBSTRATE

The basic unit which determines the rates is the enzyme-substrate system. The quantities of enzyme and of substrate together limit the maximum rates which can be reached under any given conditions. Such maximum rates are exceptional under physiological conditions, the limiting factor being usually, but not always, the amount of substrate: the fact that intermediate products do not usually accumulate shows that the substrates of the intermediary enzymes are removed as rapidly as they are formed. The average half-life of the acids of the tricarboxylic acid cycle in a rapidly respiring tissue is a few seconds [6]. The amounts of enzyme in the tissue are sufficient to deal with the intermediates as soon as they arise; in other words, the amount of available substrate is the factor limiting the rate at which the intermediary step proceeds.

This conclusion is borne out by the fact that

addition of the intermediates often increases the rate of intermediary processes. The intermediates of the tricarboxylic acid cycle, for example, all stimulate the rate of respiration of suitable tissue preparations [7]. This indicates that the enzymes attacking the added substrates are not used to full capacity when endogenous substrates, such as glucose, are oxidized. That analogous considerations apply to the anaerobic lactic acid fermentation is shown by the fact that animal tissues can form lactic acid more rapidly from hexose diphosphate than from glucose [8].

PACEMAKERS OF METABOLISM

Although, then, the rate of many intermediary steps of metabolism depends mainly on the concentration of the substrates, this is not true for all steps. There are some reactions, though comparatively few, where the rates depend on factors other than the amounts of enzyme or substrate. These are the 'pacemakers' of metabolism: they are the reactions which are evidently of special interest in relation to the control of metabolism. Their study presents two main problems: the first is the identification of the pacemakers, the second, the analysis of the mechanism by which their rates are controlled.

There is a general principle that may guide the search for pacemakers. As pacemakers are reactions of variable rates, the level of substrate concentration of the pacemaker must vary with the rate. It must increase when the reaction rate decreases, though whether the rise is appreciable would depend on the equilibrium position of the preceding step. The study of the concentration level of intermediary metabolites, especially the change of steady-rate concentrations caused by a change of environmental conditions, may therefore provide information on the nature of pacemakers and control mechanisms. F. Lynen [2, 9], for example, found that the change from aerobic to anaerobic conditions in fermenting yeast cells is accompanied by a rise in orthophosphate within the cells, which indicates that a reaction involving phosphate is one of the pacemakers of fermentation. Information on the steady-state levels of intermediary metabolites is still very limited, however, owing to lack of adequate methods of analysis. Several laboratories are now engaged in elaborating analytical techniques [4, 11, 12].

PACEMAKERS OF ANAEROBIC GLYCOLYSIS

Of the twelve major steps of anaerobic glycolysis (figure 1), two have been assumed by various

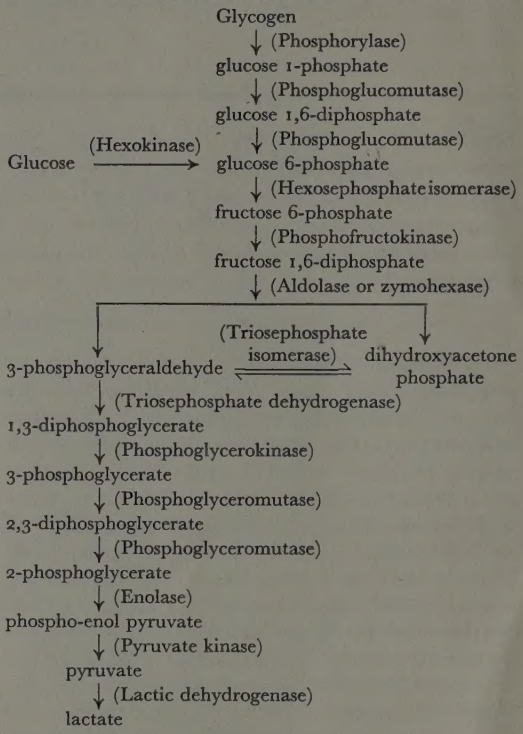

FIGURE 1 – *Lactic acid fermentation (anaerobic glycolysis). Intermediary changes of the carbon skeleton of carbohydrates. The enzymes concerned in the various stages are shown in brackets.*

authors to act as pacemakers of anaerobic glycolysis. The first is the hexokinase reaction [8], by which glucose is converted to glucose 6-phosphate, ATP acting as the phosphorylating agent. This reaction probably initiates all major metabolic reactions of glucose: the anaerobic fermentation, the complete oxidation, and the transformations into glycogen, fat, amino acids, or other cell constituents (figure 2). While the hexokinase reaction (or a reaction very closely connected with it, possibly the penetration of glucose to the site of hexokinase) evidently determines the rate of glucose consumption, it cannot control the energy production from glucose because of the variety of pathways open to glucose 6-phosphate.

The triosephosphate dehydrogenase reaction has been taken to be the second pacemaker which decides the rate of energy production from glucose 6-phosphate. This is a complex reaction in which diphosphopyridine nucleotide, adenosine phosphate, and orthophosphate take part (figure 3). It is obvious from the formulation that the reaction

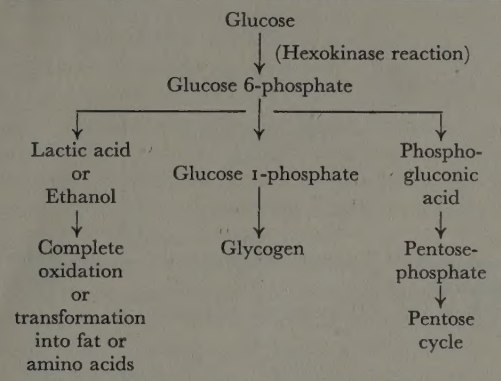

FIGURE 2 – *Diagrammatic presentation of the alternative pathways of metabolism open to glucose and glucose* 6*-phosphate.*

cannot take place unless adenosine diphosphate and phosphate are available—the very two substances which become available when energy is spent. It must be understood, however, that the rate control is due not so much to the presence or absence of these reactants as to the level of their concentrations: the rate decreases even before adenosine diphosphate or phosphate disappears completely. It also follows that the rate of the triosephosphate dehydrogenase reaction may be

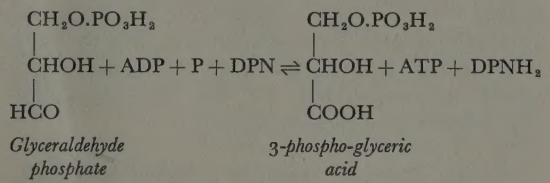

FIGURE 3 – *Overall change in the triosephosphate dehydrogenase systems. This is the result of two major steps, catalysed by triosephosphate dehydrogenase and by phosphoglycerokinase respectively (Bücher* [10]).

influenced by any process which either removes or supplies adenosine diphosphate or phosphate. The main reaction which removes these two reagents is respiration, coupled with oxidative phosphorylation. Hence respiration must inhibit fermentation; this is the interpretation of the Pasteur effect (the inhibition of fermentation by oxygen) proposed by M. J. Johnson [1] and by F. Lynen [2]. On the other hand, any energy-requiring process will, within limits, stimulate fermentation because it generates adenosine diphosphate or phosphate.

While it is very probable that this mechanism operates, some aspects of glucose utilization remain to be clarified, as F. Lynen and R. Koenigsberger [9] have pointed out. Stoppage of the triosephosphate dehydrogenase reaction can explain stoppage of lactic acid formation, but it does not account for the decreased utilization of sugar. Non-removal of triosephosphate would lead to an accumulation of fructose diphosphate, because of the ready reversibility of the aldolase reaction (see figure 1). But the stage between fructose 1:6-diphosphate and fructose 6-phosphate is not readily reversible. Hence the accumulation of triosephosphate or fructose 1:6-diphosphate cannot, by mass action, prevent the hexokinase reaction or the conversion of glucose 6-phosphate into fructose 6-phosphate and fructose 1:6-diphosphate. On the contrary, the relatively high concentration of adenosine triphosphate required for the inhibition of the triosephosphate dehydrogenase reaction is expected to facilitate the formation both of glucose 6-phosphate and of fructose 1:6-diphosphate from glucose or from glycogen. Thus additional factors must be responsible for the decrease of sugar consumption when conditions change from anaerobiosis to aerobiosis. Lynen and Koenigsberger [9] have raised the question whether the rate of the hexokinase reaction might be controlled by the hexosephosphates formed. An important observation in this context is the non-competitive inhibition of hexokinase by glucose 6-phosphate, discovered by H. Weil-Malherbe and A. D. Bone [13] and further investigated by R. K. Crane and A. Sols [14]. Glucose 6-phosphate in as low a concentration as $0{\cdot}5 \times 10^{-3}$ M causes 40 per cent inhibition. It is certainly feasible that this inhibition, or analogous effects at other stages of glycolysis, play a part in the control mechanism, but before this can be accepted, further investigations are needed, especially of the steady-state concentrations of the phosphorylated intermediates, of the kinetics of the enzyme systems concerned, and of specific inhibitions by intermediary metabolites.

It has also been considered whether the reduction of sugar consumption in the presence of oxygen might be caused by a direct action of oxygen on an enzyme, for instance by the oxidation of an —SH group which might inactivate an enzyme reversibly [15–17, 9], but the evidence argues against this kind of mechanism. Under a variety of conditions fermentation can reach the anaerobic level in the presence of oxygen, as, for example, on addition of dinitrophenol or isonitrile.

PACEMAKERS OF RESPIRATION

When energy is released by the oxidation of carbohydrate, fat, and amino acids, there are over a hundred identifiable intermediate steps, only a

few of which are pacemakers. Pacemakers are expected at two types of stages of respiration: first, at those where the total oxygen consumption (i.e. energy supply) is determined, and secondly at those where, after a partial degradation, more than one pathway is open.

It follows from the fact that intermediates do not accumulate that those steps which initiate the oxidation of a substrate must be among the pacemakers of respiration. These reactions also decide which substrate, among a mixture, is attacked preferentially—whether carbohydrate, fatty acids, or amino acids serve as a source of energy. Branching stages, where more than one pathway can be entered by an intermediate metabolite, occur at many points. Examples are given in figure 4, which shows diagrammatically the major stages of the metabolism of carbohydrate and fatty acids where branching of pathways may take place. It is decided at these branching points whether glucose is broken down to supply energy or stored in the form of glycogen; whether glucose, via acetyl coenzyme A, is converted into fat or whether fat is broken down to give energy; whether ketone bodies are formed from fatty acids or acetyl coenzyme A or disposed of via the tricarboxylic acid cycle; whether intermediates of the tricarboxylic acid cycle are oxidized, or used to supply carbon skeletons for the synthesis of amino acids, porphyrins, or steroids.

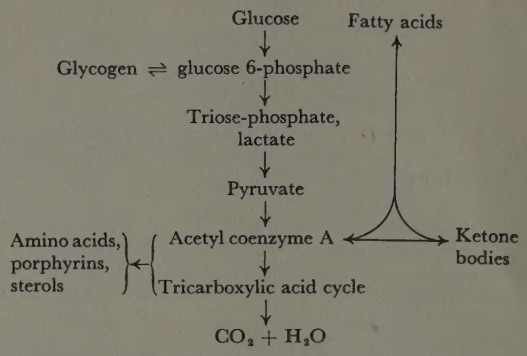

FIGURE 4 – *Examples of branching points in the intermediary metabolism of carbohydrates and fatty acids.*

ENZYMIC PATTERN OF CONTROL MECHANISM

The analysis of the control mechanisms which operate in these pacemaker reactions must begin with a translation of the situation into the terminology of enzyme chemistry. Two types of situation may be distinguished. Alternative metabolic routes may arise either from a choice of alternative reactions (say breakdown of either carbohydrate, or fat, or protein when energy is needed), or from a choice of alternative directions of pathways (say synthesis or breakdown of fatty acids). In the first case the reactions which take place are essentially different; in the second the same reactions move in opposite directions.

Closer examination of the first case shows that the alternative reactions which occur when cells have the choice of obtaining energy from a variety of substrates are not entirely independent processes. The oxidation of a substrate by molecular oxygen generally involves three types of catalysts, arranged in series. They are respectively the pyridine nucleotides, flavoproteins, and iron porphyrins. Only the first step of this complex sequence varies from substrate to substrate. All other intermediate steps are shared by the alternative reactions, as shown diagrammatically in figure 5. Five substrates, representing the great majority of metabolites supplying energy, are chosen to illustrate the principle. The oxidation begins in every case with a transfer of hydrogen atoms to a common reagent, diphosphopyridine nucleotide.

Partial exceptions are fatty acids and succinate, but in these cases most intermediate steps are also shared with the other substrates. Fatty acids and succinate donate hydrogen atoms directly to a flavoprotein, a deviation from the general rule which is necessitated by the thermodynamic characteristics of these substrates.

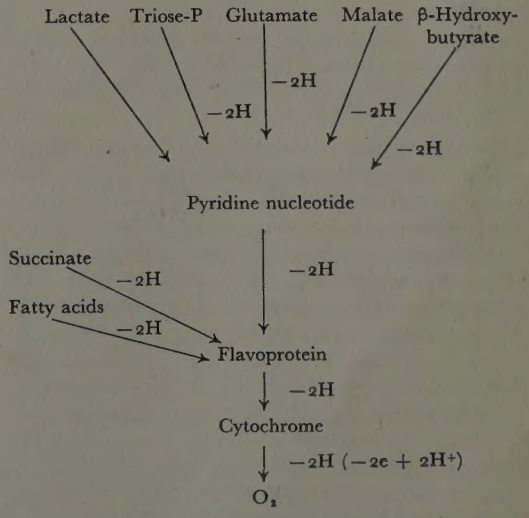

FIGURE 5 – *Joint pathways of hydrogen transport from different substrates to molecular oxygen.*

Choice of substrate thus means competition of several substances for the same catalyst. The majority of substrates compete directly for diphosphopyridine nucleotide: fatty acids, succinate, and reduced diphosphopyridine nucleotide compete for flavoprotein. Which substrate is oxidized depends on definable physico-chemical properties such as the relative rates at which the substrates interact with the common agent.

Of a similar type, also involving competition, seems to be the control mechanism at one of the branching points of metabolism where the fate of acetic acid, reacting in the form of acetyl coenzyme A, is determined. Among the major pathways open to acetyl coenzyme A in liver tissue is the conversion into acetoacetate (ketogenesis) or the complete oxidation to carbon dioxide and water through the tricarboxylic acid cycle (antiketogenesis) (figure 4). Acetoacetate arises by condensation of two molecules of acetate, while the oxidation via the tricarboxylic acid cycle requires condensation of acetate with oxaloacetate. This suggests that the availability of oxaloacetate is the key factor in controlling ketogenesis and antiketogenesis [18]. However, experimental tests in the intact organisms failed in many cases to bear out this view: succinate, which readily supplies oxaloacetate in the body, does not relieve acidosis in human diabetics [19] or in the rat [20]. Some decrease in urinary ketone body excretion in rats made ketotic by excess butyrate occurs, however, when various precursors of oxaloacetate are administered by stomach tube [21]. On the other hand, oxaloacetate is certainly antiketogenic in isolated mitochondria. Fatty acids yield ketone bodies in liver mitochondria in the absence of oxaloacetate, but they are oxidized through the tricarboxylic acid cycle when oxaloacetate is added [22]. The availability of oxaloacetate can thus, at least under certain conditions, decide whether ketone bodies accumulate or fatty acids are completely oxidized.

Experiments with substances which interfere with the tricarboxylic acid cycle, and thereby reduce the supply of oxaloacetate, lead to the same conclusion. Malonate, which prevents the oxidation of succinate, and ammonium ions, which divert α-ketoglutarate to glutamate, are both ketogenic [23]. These are observations which point to the key role of oxaloacetate, but it cannot be claimed that the mechanism controlling ketogenesis is fully understood, seemingly because of insufficient information on the factors which control the steady-state level of oxaloacetate. At least five independent reactions are known to cause the formation or disappearance of oxaloacetate:

malate + DPN	⇌ oxaloacetate + $DPNH_2$ (malic dehydrogenase)
phosphopyruvate + CO_2 + ADP (or IDP)	⇌ oxaloacetate + ATP (or ITP) (Utter-Kurahashi reaction)
aspartate + α-keto-glutarate	⇌ oxaloacetate + glutamate (transaminase)
oxaloacetate + H_2O	⇌ pyruvate + HCO_3^- (oxaloacetic decarboxylase)
oxaloacetate + acetyl coenzyme A	⇌ citrate + coenzyme A (condensing enzyme)

The steady-state level of oxaloacetate must depend on the interplay of these five (and possibly other) reactions, but how this interplay is governed is unknown. Summing up, it can be said that the metabolic fate of acetyl coenzyme A at one of the branching points is decided by the supply of a special reactant. Again one substrate competes between two alternatives, either a reaction with oxaloacetate or a reaction with the second molecule of acetyl coenzyme A.

The availability of oxaloacetate can account for the formation or non-formation of acetoacetyl coenzyme A. Free acetoacetate appears in appreciable quantities only in liver. This is accounted for by the fact that liver contains an enzyme which hydrolyses acetoacetyl coenzyme A (deacylase) and, unlike most other tissues, cannot convert free acetoacetate back to the coenzyme A derivative [24]. This illustrates the obvious point that presence or absence of specific enzymes contributes to the control of pathways.

The cases so far considered have been concerned with the mechanisms by which alternative pathways of metabolism are selected. There is another pattern of enzymic mechanism, however, when the alternatives are different directions of the same reaction: an example is the synthesis or breakdown of fatty acids. Long-chain fatty acids are broken down and built up by the removal or addition of C_2- units reacting in the form of acetyl coenzyme A. In breakdown and synthesis there are four reversible reactions for each molecule of acetyl coenzyme A [25, 26]. In breaking down, the first step is the dehydrogenation of the fatty acid chain in the α-β position, leading to the formation of an α-β double bond, the immediate hydrogen acceptor being a flavoprotein:

$$\underset{\text{(acyl coenzyme A)}}{R.(CH_2)_n.CH_2.CH_2.CH_2.CO.S—CoA} + \text{flavoprotein}$$

$$\Downarrow$$

$$\underset{\text{(α-β unsaturated acyl coenzyme A)}}{R.(CH_2)_n.CH_2.CH{=}CH.CO.S—CoA} + \text{dihydroflavoprotein}$$

The second step is hydration of the double bond, leading to a β-hydroxy acid:

$$\underset{\text{α-β unsaturated acyl coenzyme A}}{R.(CH_2)_n.CH_2.CH{=}CH.CO.S{-}CoA} \overset{+H_2O}{\underset{-H_2O}{\rightleftharpoons}} \underset{\text{β-hydroxy acyl coenzyme A}}{R.(CH_2)_n.CH_2.CH(OH).CH_2.CO.S{-}CoA}$$

This is followed by the dehydrogenation of the β-hydroxy acid to a β-ketonic acid, with DPN as the primary hydrogen acceptor:

$$\underset{\text{β-hydroxy acyl coenzyme A}}{R.(CH_2)_n.CH_2.CH(OH).CH_2.CO.S{-}CoA} + DPN \quad \Downarrow \quad \underset{\text{β-keto acyl coenzyme A}}{R.(CH_2)_n.CH_2.CO.CH_2.CO.S{-}CoA} + DPNH_2$$

The fourth step is the 'thiolysis' of the β-ketonic acid by a molecule of coenzyme A, yielding acetyl coenzyme A and an acyl coenzyme A with two carbon atoms less than the original:

$$\underset{\substack{\text{β-keto acyl}\\ \text{coenzyme A}}}{R.(CH_2)_n.CH_2.CO.CH_2.CO.S{-}CoA.} + CoA{-}SH \quad \Downarrow \quad \underset{\text{acyl coenzyme A}}{R.(CH_2)_n.CH_2.CO.S{-}CoA} + \underset{\text{acetyl coenzyme A}}{CH_3.CO.S{-}CoA}$$

In reverse, these four reactions lead to the elongation of fatty acids, and the question arises of what determines whether synthesis or degradation occurs in the reversible system. The sum of the four reactions causing shortening or lengthening of fatty acid chains is as follows:

$$C_n\text{-acyl CoA} + DPNH_2 + \text{reduced flavoprotein} + \text{acetyl CoA} \rightleftharpoons C_{n+2}\text{-acyl CoA} + DPN + \text{flavoprotein} + CoA$$

Being reversible, the reaction proceeds from left to right when the values for the three ratios

$$\frac{\text{acetyl CoA}}{\text{CoA}}, \quad \frac{\text{reduced flavoprotein}}{\text{oxidized flavoprotein}}, \quad \frac{DPNH_2}{DPN}$$

are relatively high, and from right to left when the ratios are relatively low. In the intact body, fat is generally synthesized when there is a surplus of carbohydrate, i.e. when pyruvate is available to form more acetyl coenzyme A than is required for energy production by the tricarboxylic acid cycle. Concomitant with the formation of acetyl coenzyme A from pyruvate occurs the reduction of diphosphopyridine nucleotide and, indirectly, of flavoprotein. Thus excess of pyruvate raises the above three ratios, whereas lack of carbohydrate lowers them. It can therefore be understood, in general terms, why fatty acids are broken down in the absence, and synthesized in the presence, of carbohydrate. It can also be understood why fat synthesis is impaired in diabetes and why insulin is necessary for fat synthesis [5]. The utilization of carbohydrates in higher organisms requires the presence of insulin: hence absence of insulin reduces the oxidative formation of pyruvate, which in turn reduces the supply of acetyl coenzyme A and lowers the ratio $DPNH_2/DPN$ [28].

There are other syntheses in which the mechanisms controlling the balance between synthesis and breakdown cannot yet be satisfactorily visualized, mainly because the enzymic reactions have not been sufficiently clarified. The principles operating in the fatty acid system are probably factors in many cases.

The pacemakers of respiration so far considered illustrate the manner in which the choice between alternative metabolic processes can be controlled. There remains to be discussed the mechanism which regulates the rate of oxygen consumption or aerobic energy supply. This is determined by the reactivity of the system of catalysts which governs the oxidation of organic substrates by molecular oxygen; in other words, by the rate at which reduced diphosphopyridine nucleotide, reduced flavoprotein, and reduced cytochrome transmit hydrogen atoms or electrons to O_2. The hydrogen-transport from reduced diphosphopyridine nucleotide to O_2, along the path outlined in figure 5, is known to be coupled with the synthesis of adenosine triphosphate from adenosine diphosphate and orthophosphate. Owing to this coupling, the reaction

$$DPNH_2 + \tfrac{1}{2}O_2 \longrightarrow DPN + H_2O$$

and its component steps, proceed at full rate only if adenosine diphosphate and orthophosphate are present (although short cuts not involving phosphates may occur under special circumstances [26]). In fact, the oxidation of reduced diphosphopyridine nucleotide as formulated above is a 'part reaction', and a more correct representation of the position is given by the following scheme:

$$\left.\begin{matrix} DPNH_2 + \tfrac{1}{2}O_2 \\ + 3ADP + 3P \end{matrix}\right\} \longrightarrow \left\{\begin{matrix} DPN + H_2O \\ + 3ATP + 3H_2O \end{matrix}\right.$$

This coupling of oxidation and phosphorylation (oxidative phosphorylation) seems to be obligatory under physiological conditions, and the role of phosphate in this system is therefore comparable to that in the triosephosphate dehydrogenase reaction mentioned earlier. Both reactions depend on the supply of adenosine diphosphate and phosphate, and are thus controlled by the rate at

which adenosine triphosphate is split to adenosine diphosphate and phosphate, i.e. by the amount of energy spent. As the rate of the interaction between substrates and diphosphopyridine nucleotide depends on the rate at which diphosphopyridine nucleotide is regenerated by the oxidation of reduced diphosphopyridine nucleotide, oxidative phosphorylation also controls the rate of degradation of the substrate.

These concepts are tentative. They are supported by substantial evidence, but cannot be regarded as established in detail. What is well established is the rate-limiting function of phosphate and/or phosphate acceptors under certain well-defined conditions. Earlier observations by A. Lennerstrand [29] and V. A. Belitzer [30] on rate control by phosphate and/or phosphate acceptors have been elaborated in particular by H. A. Lardy and H. Wellman [31], who showed that the rate of oxidation of a variety of substrates in liver mitochondria is accelerated by the addition of inorganic phosphate and of adenosine diphosphate or other phosphate acceptors [3, 4, 32–34]. Under some experimental conditions the rate-limiting factor is inorganic phosphate, under others it is the phosphate acceptor [35]. It is probable that *in vivo* both can play a role.

PACEMAKERS AS VULNERABLE STAGES OF METABOLISM

When specific chemicals, such as hormones, or drugs, or poisons, modify metabolic rates, it is likely that the point of attack is one of the pacemakers [36]. The primary effect of such agents is in most cases either inhibition or activation of an enzyme. Since the activity of non-pacemakers is not a factor limiting the rate, even a major inactivation or an activation of a non-pacemaker would not change overall metabolic rates, although it may change the level of the steady-state concentrations of intermediates.

Experimental observations agree with the view that the stages of cell metabolism liable to be influenced by inhibitors or hormones are usually the pacemaker reactions. Specific inhibitors of glycolysis interfere either with the hexokinase reaction (e.g. L-glyceraldehyde) or with the triosephosphate dehydrogenase system (e.g. iodoacetate). Specific inhibitors of respiratory processes interfere either with the electron-transport system (e.g. cyanide, azide, or sulphide) or with the step initiating the attack on the organic substrate, i.e. the dehydrogenase reaction (e.g. malonate). Other inhibitors upset the balance of reactants at branching points, for example the ketogenic agents which reduce the supply of oxaloacetate in the liver. As for hormones, insulin is taken to control the rate of the hexokinase reaction, possibly indirectly by controlling the entry of sugar into the cells. The effect of thyroxin or triodothyronine on the basal metabolic rate seems to be due to interference with the electron-transport system. The glycogenolytic action of adrenaline is due to an acceleration of phosphorylase, the enzyme which initiates the degradation of glycogen [37]. In all the examples the point of attack is a pacemaker reaction.

GENERAL COMMENTS ON THE DESIGN OF THE 'PRIMITIVE' CONTROL MECHANISMS

If the hormonal control of biological activities operates generally through an effect of the hormone on the activity of an enzyme, the non-hormonal control mechanisms discussed in this paper are in principle of a different kind. They usually belong to the type of systems which engineers call 'feedback' systems. Control by feedback is an arrangement in which the controlled process, as it progresses, creates conditions unfavourable for further progress, and thereby causes the rate to slow down. This slowing down recreates more favourable conditions and thereby speeds up the progress. Thermo-regulators are among the simplest examples of feedback systems.

Mechanisms controlling metabolic rates include in many cases arrangements of this type. The key substances through which the controls governing the energy supply are operated are inorganic phosphate and adenosine diphosphate. Their presence stimulates the rate of both the aerobic and the anaerobic degradation of foodstuffs. When energy is spent, the concentrations of these two substances are bound to rise. The increased rate of respiration or fermentation in turn causes their removal and thereby eventually decreases the rates of the energy-supplying reactions.

Competitive mechanisms, in which diphosphopyridine nucleotide is one of the key substances, may also be looked upon as feedback systems. When two substrates compete for a common intermediary catalyst, each by its presence creates unfavourable conditions for the reaction of the other substrate. As one of the substrates disappears, the second is automatically 'fed' to the catalyst, so that approximate constancy of catalytic activity is secured.

The relative contributions made in higher animals by hormonal control and feedback

control may be illustrated by the example of the energy-supplying reactions. While hormones, in particular that of the thyroid, play an important role in the control of the basal metabolic rate, the energy needs due to functional activity, such as contraction by muscles or secretion by glands, are primarily controlled by feedback mechanisms. It is true that hormones may control secretion and thereby influence the rate of energy supply, but these effects of hormones on the rates of energy supply are probably indirect and achieved through the mediation of feedback mechanisms.

Feedback mechanisms occur at many levels of biological organization. The long-known effect of the alveolar carbon dioxide pressure on breathing [38] is an example. Others concern the heart beat [39] and especially the activities of the nervous system, including those of the higher centres. The purposeful behaviour of biological systems in particular can in many cases be accounted for in an entirely mechanistic manner by hypotheses based on the feedback principle [40].

So far, no more than a beginning has been made in the elucidation of the basic chemical mechanisms which control the nature and the rate of metabolic processes, but an insight has already been gained into some of the principles involved. The adaptation of the reaction rates to changing needs can be understood, at least in part, on the basis of the properties of the enzyme systems, inhibitions and feedback arrangements being the distinctive features of the control mechanisms.

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Macquer, the first lexicographer of chemistry

DOUGLAS McKIE

Macquer's *Elémens de chymie théorique* (1749) and his *Elémens de chymie-pratique* (1751) established him as the leading French writer on chemistry and the successor of Nicolas Lemery. But his greatest work—his dictionary, virtually an encyclopaedia —came fifteen years later. This passed through many editions, both in French and in translation into foreign languages, and had a powerful effect on the development of chemistry at a time of revolutionary change.

Pierre-Joseph Macquer, one of the distinguished chemists produced by eighteenth-century France, was born in Paris on 9th October 1718, the elder of the two sons of Joseph Macquer and his wife, Marie-Anne Caillet. Philippe, his younger brother, was born on 15th February 1720. His father was said to be descended from a noble Scots family who had taken refuge in France after having lost all their possessions through their devotion to the Catholic faith and the Stewart cause. Macquer does not seem, however, to be either a Scots name or a corruption of one; nor would it appear to have been derived from Ker, since the noble families of that name were not supporters of the Stewarts. The writer has suggested elsewhere [1] that Macquer is a corruption of Maguire, the family name of the ill-fated house of Enniskillen. Many of the Jacobite entries in the parish registers of Saint-Germain-en-Laye, where James II and his court found refuge, agree with this suggestion; thus it seems probable on the evidence that Macquer was of Irish rather than Scottish descent.

It is said that the Macquers insisted that their sons should take up professions. Such insistence probably came from the father, with memories of a half-century of poverty among his fellow exiles. Philippe, the younger brother, elected for the law, but, on account of his ill health, eventually turned to history and literature, and in these subjects became well known for the exactness of his scholarship and the clarity of his literary style. Pierre-Joseph, on the other hand, chose medicine; not, it would seem, through any deep love of that art, but because it disagreed less than any other calling with his growing taste for the physical sciences. In 1742, at the age of 24, he graduated doctor of medicine in Paris. He had, however, been specially interested in chemistry, and in 1745 he was elected to the *Académie des Sciences* as *adjoint-chimiste*, in succession to Paul-Jacques Malouin, who had been promoted *associé*. Macquer himself became *associé* in 1766 and *pensionnaire* six years later, in 1772. He served as deputy director of the *Académie* in 1773 and as director in 1774.

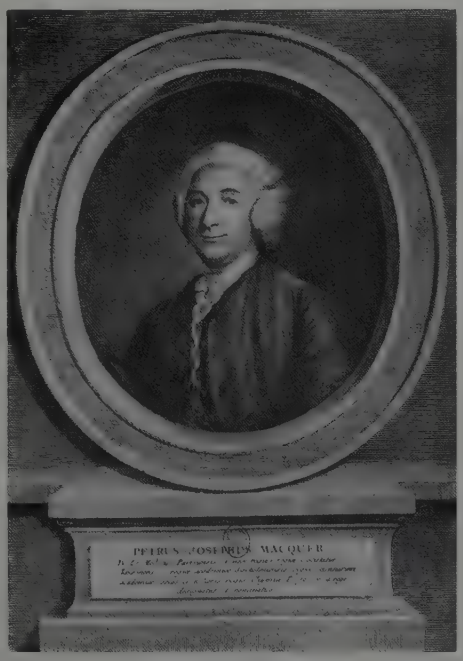

FIGURE 1 – *Pierre-Joseph Macquer* (1718–84), *Professor of Chemistry in the* Jardin du Roi *in Paris, and first lexicographer of chemistry. From an engraving by Benoist after a portrait by Garrand.* (*Courtesy of the* Bibliothèque Nationale, *Paris.*)

Macquer studied chemistry at the *Jardin du Roi* under Guillaume-François Rouelle (1703–70), an account of whose work and teaching has already been given in this journal [2]. Rouelle was regarded by his French contemporaries as the founder of chemistry in France, where he had introduced and taught the phlogiston theory, which, in spite of what has been said against it by those who have not fully grasped

its role in the historical development of chemistry, had the great merit of taking chemistry out of the hands of the alchemist and the apothecary. Rouelle's chemistry was, however, not entirely free from some of the familiar characteristics of the apothecary's art: it was at the hands of Rouelle's pupil, Macquer, that French chemistry finally lost these features and became a science that stood on its own. To this important and significant change Macquer contributed both by his teaching and by his numerous books. Before turning to consider these, however, it would be appropriate to devote a little time to his early researches.

FIGURE 2 – *An engraving—probably by Benoît Audran* (ob. 1772), *after a painting by Teniers of an alchemist in his laboratory—from the first page of the text of the second edition* (*quarto*) *of Macquer's* Dictionnaire de Chimie (*Paris*, 1778).

His first published memoir in the annual volume of *Mémoires de l'Académie* dealt with the solubility of oils in spirit of wine (1745). Then followed two other memoirs on salts of arsenic (1746 and 1748) and another on chalk and plaster (1747). In a paper on Prussian blue (1752) he showed that this substance was a combination of iron with something that the alkalis extracted from the animal matters used in its preparation. For over thirty years similar publications continued—on dyestuffs, fusible earths, platinum, the solubility of salts in spirit of wine, mineral waters, and similar topics. In the meantime, however, Macquer had begun to teach the subject that had captured his whole interest and attention.

In 1757, in collaboration with Antoine Baumé (1728–1804), Macquer began to give courses on chemistry in their laboratory in the rue Saint-Denis, Paris. Baumé was a master-apothecary and was demonstrator in chemistry at the college of pharmacy: he was the author of many papers and books. Notable among the latter is his *Chymie expérimentale et raisonnée* (Paris, 3 vols, 1773), in which he embodied the results of sixteen of these annual courses given in association with Macquer; in each of these more than two thousand experiments were demonstrated. Macquer himself, in 1770, obtained from Buffon the reversion of Bourdelin's chair of chemistry in the *Jardin du Roi*, took the oath in 1771, and succeeded to the chair on Bourdelin's death in 1777.

Macquer's *Elémens de chymie théorique* first appeared in 1749 in Paris. It was a small octavo single volume of about 350 pages, with three plates of chemical apparatus and a reproduction of Geoffroy's table of chemical affinities. When the most famous of all textbooks of chemistry, the *Cours de chymie* of Nicolas Lemery (1645–1715), which had first appeared in 1675 in Paris, was still current in one or other of its many revised editions, not only in France but also throughout Europe in translations into English, German, Latin, Italian, and Spanish, and when the great quarto edition (Paris, 1756) of nearly 1000 pages was still to come, Macquer's modest little book must have seemed a slight affair. But it dealt with the principles of chemistry and with the different classes of chemical substances and their chemical properties; significantly, it said nothing about their pharmaceutical properties, in spite of what might have been expected from Macquer's interests as a physician. Rouelle's teaching, it would appear, had here achieved one of its most important consequences, and the success of this new writer on chemistry, whose approach was so different in that he presented his subject as an independent branch of natural knowledge and as a science in itself, was immediate.

Two years later, a further work by Macquer appeared, the *Elémens de chymie-pratique* (Paris, 1751), in two octavo volumes with a total of over 1000 pages. A new edition of the earlier book on theoretical chemistry followed in 1753. Then in 1756 there was a new edition of that book in one volume and one of the book on practical chemistry in two volumes, forming altogether three volumes of some 1500 pages. Macquer had now taken his place as the leading French writer on chemistry and his reputation grew quickly. An English version of his book, under the title 'Elements of the

Theory and Practice of Chemistry', translated by Andrew Reid, appeared in two octavo volumes in London in 1758; there was a second edition in 1764, dedicated to the Earl of Bute. A third edition in three volumes was published in Edinburgh in 1768. This was dedicated 'To the STUDENTS at the UNIVERSITY of EDINBURGH and all other LOVERS of CHYMISTRY'; it remains one of the most attractive of all the editions of this work. Another English edition, probably a fourth, has been reported as published in London in 1775. A fifth edition, in one volume, came out in Edinburgh in 1777: a copy of this edition is now before the present writer, with two loose slips carrying notes apparently in the hand of Joseph Black, to whom it may have belonged. Indeed, the appearance of the editions of 1768 and 1777 in Edinburgh may be connected with Black's very strong recommendation of Macquer's book to the students attending his chemistry class in the University. Black placed Macquer's 'Elements' first among 'the most necessary books', according to a student's notes taken down from Black's lectures, and he added that the work 'contains a clear and concise account of most of the facts relating to chemistry'. The author [3] has shown elsewhere that Black was recommending this book to his students as early as the university session of 1767–68. The *Elémens* was translated also into German, Dutch, and Russian.

It is, however, for his *Dictionnaire de chymie* (Paris, 1766, 2 vols, octavo), the first of its kind, that Macquer will always be remembered. Although he was already established as a writer, the first edition of this book appeared anonymously. It was a considerable work of some 1300 pages, but it was less a dictionary than a compact treatise on the science of chemistry, with the details presented in a series of about 500 articles arranged alphabetically. A reimpression of this first French edition followed in 1769, a Swiss edition in three volumes having been published meanwhile in 1767. An English translation in two volumes by James Keir (1735–1820) appeared in London in 1771; a second edition of this followed in 1777, in three volumes with an appendix consisting of a treatise on the various kinds of permanently elastic fluids or gases. German, Danish, and Italian versions appeared later. A further Swiss edition appeared in Neuchâtel in 1789 in five volumes, the fifth volume being a supplement dealing with more recent advances.

Further issues of a second French edition were published in Paris in 1778, an edition described as second having, however, come out in three volumes in 1777. The edition of 1778 appeared in two formats, one of four octavo volumes and the other of two handsome quartos. The latter came from the *Imprimerie de Monsieur*, that is, from the press of which the elder of the King's brothers, the Comte de Provence, was patron. This quarto edition is one of the most beautifully produced of all works on chemistry and is still a collector's piece. An engraving of Teniers' picture of an alchemist in his laboratory, from the opening page of the text, is reproduced in figure 2. Its two volumes contain nearly 1600 pages, including an index in double columns running to 200 pages; this was necessary because of the book's encyclopaedic character.

Comparison of the two French editions of 1766 and 1778 shows that in the latter many of the earlier articles were greatly extended and also that many new ones were included, as was necessary in view of the great developments in chemistry that had taken place between these dates. To appreciate these revolutionary changes in chemical knowledge we need merely to recall that it was only in 1766, the year of the first edition, that Cavendish had isolated and recognized 'inflammable air' (hydrogen) and that the discovery of the gases had then rapidly opened up a whole new field of pneumatic chemistry, especially at the hands of Priestley. In the second edition, therefore, there were about fifty new articles, besides, as we have noted, much additional matter inserted in the text of those published in the first edition.

The modern reader interested in the history of chemistry instinctively turns to certain articles in a work of this kind. One of these will probably be that dealing with the chemical elements. Macquer, in 1766, is singularly modern in what he says: 'Those bodies are called by chemists *elements*, which are so simple, that they cannot by any known method be decomposed, or even altered; and which also enter as principles, or constituent parts, into the combination of other bodies, which are therefore called compound bodies.' However, in the next sentence the reader will find that Macquer has the ancient four-element theory in mind: 'The bodies in which this simplicity has been observed are fire, air, water, and the purest earth; for by the most complete and accurate analyses which have been made, nothing has been ever ultimately produced but some one, or more, of these four substances, according to the nature of the decomposed bodies. These substances, although reputed simple, may possibly not be so, and may even result from the union of several

other more simple substances: but as experience teaches us nothing on this subject, we may without inconvenience, and we ought to consider, in chemistry, fire, air, water, and earth, as simple bodies; because they really act as such in all chemical operations.' This was repeated in the second edition; in fact Macquer, in the absence of more exact knowledge, continued to accept the four-element theory, although making use of Boyle's definition of a chemical element.

The short article on alchemy is interesting, and we may quote it in full: 'This term has been employed by the pretended adepts, and by searchers after the philosopher's stone, to distinguish that kind of chemistry, the knowledge of which they flattered themselves was reserved for them alone. The adepts consider chemistry as a vulgar science, which scarcely contains the first elements of the mysterious science of alchemy. But hitherto they have produced nothing which, in the judgment of sensible men, can give the least grounds for such a pretention. True chemists consider alchemy as an imaginary science, and those who are devoted to it as persons who, from want of better instruction, quit a reality for the sake of a shadow.' The reader may thus be led to 'Adept', and he will find that this 'is the name assumed by those alchemists who claim to have discovered the secret of the philosopher's stone. See *Philosopher's Stone*.' On turning to the latter reference the reader will find that 'This name is given by alchemists to the preparation by which metals may be transmuted, gold and silver made, and all the wonders produced of (what they call) the *great work*.' Macquer's views about alchemists are clear from these quotations.

If we turn to the articles relevant to the contemporary struggle between the phlogiston theory and the new chemistry that was then being developed by Lavoisier, we find that Macquer had propounded a compromise between the old and the new. He was unwilling to abandon what the accepted theory of chemistry taught—namely, that in combustion and calcination phlogiston was set free from burning bodies and calcined metals—and yet was forced to consider the new experimental evidence adduced by Lavoisier that the gain in weight of metals on calcination was due to their combination with a part of the air. Macquer therefore continued to assert that phlogiston, which he regarded as the matter of light, was set free in combustion and calcination, and that, while this admittedly led to a decrease in weight, the loss was more than made up by concurrent combination with air. This was a considerable modification of the phlogiston theory as originally propounded and as accepted in Macquer's time; it took Lavoisier's most skilful criticism and experimentation to refute such a compromise embracing both theories.

As Macquer's teaching and his writing had both been marked by clear and logical presentation, and as he had always had the reputation of opposing speculation that went beyond facts, it was most unfortunate that he should have been compiling his great dictionary during the most active years in which the new chemistry was arising from the old. Those who study his work closely are led to conclude that, but for his death in 1784 before the revolution in chemistry was complete, he might very readily have accepted the newer ideas. His dictionary of chemistry was the first of its kind, and it became a model of all those that have followed since. Nicholson's 'Dictionary of Chemistry' (London, 2 vols, 1795), the first dictionary of chemistry compiled in Britain, was constructed from Macquer's, and others that have since been produced here and elsewhere have followed the same model.

Macquer was much interested in the applications of chemistry. His well-known competence in such matters led to his appointment as director of the royal porcelain factory at Sèvres in 1766 in succession to Hellot, whom he succeeded also as director of the dyeing industries. He worked with Lavoisier and others on the official investigation into methods of improving and increasing the national production of saltpetre for the manufacture of gunpowder. He had also worked with Lavoisier when the latter was first studying the combustion of the diamond, and had earlier observed the slight flame produced when diamond was burnt. He had noticed too that the burning of a flame of 'inflammable air' against a cold surface produced drops of a liquid that appeared to be water.

Macquer died suddenly on 15th February 1784, in Paris.

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Mammalian spermatozoa

M. W. H. BISHOP and C. R. AUSTIN

Many branches of scientific enquiry have contributed to our knowledge of the spermatozoon and its functions. Its story is that of a highly specialized cell that can neither grow nor divide; that consists essentially of a condensed nucleus with means for locomotion and for penetrating the egg; that plays no role in the physiology of the animal that produces it; that is solely concerned with the production of new individuals of the kind from which it arose.

About 280 years ago, Johan Hamm of Arnhem saw spermatozoa in human semen and communicated his discovery to the eminent seventeenth-century microscopist Anton van Leeuwenhoek. Within a few years Leeuwenhoek and others had observed spermatozoa in the semen of many animals, but their nature and function remained subjects of bitter dispute for nearly 200 years. They were variously thought of as structures arising from putrefaction or chemical action; as parasites or adventitious infusoria; as specialized bodies whose function was merely to stir the semen or to arouse sexual desire in the male; and as the seed from which the future embryo would grow. Leeuwenhoek subscribed to the last of these views, and believed that spermatozoa developed into embryos after nidation within the egg. Spallanzani, however, concluded from his ingenious experiments in 1780 that spermatozoa did not play a vital role in reproduction; he considered that the seminal plasma was the agent that stimulated the egg to development. This was refuted by Prévost and Dumas in 1824; they showed that fertilization is a function of the spermatozoa. In 1841 Kölliker clearly demonstrated that spermatozoa are a normal and characteristic product of the testis and that they arise by proliferation and differentiation from the testicular tissue. Proof that spermatozoa are cells, consisting of nucleus and cytoplasm, was brought forward 24 years later by Schweigger-Seidel and La Valette St George. In 1843 Barry recorded the presence of spermatozoa within the rabbit egg, and then Nelson and Newport described the actual entry of spermatozoa into the eggs of the frog and the nematode *Ascaris*. Van Beneden in 1875, and Hertwig in 1876, gave the first clear accounts of the union between a nucleus formed from the spermatozoon and the egg nucleus; they maintained that this union was the cardinal feature of fertilization. Within a few years Flemming identified the chromosomes and described the process of mitosis. By 1890 the maturation of the gametes, fertilization, and the role of chromosomes were understood in principle and also in some detail.

The microscopes available to Leeuwenhoek and his contemporaries were crude by modern standards, and in consequence the early pictures of spermatozoa were often bizarre (figure 6), but sometimes remarkably good in view of the equipment used. Some observers reported that they could see alimentary tracts (figure 1), and other organs in spermatozoa, and even described and portrayed complete diminutive embryos or homunculi (figure 2). By 1890 the conventional light microscope had reached a state of development that can scarcely be bettered today, and painstaking investigations of spermatozoon morphology were undertaken, notably by Ballowitz and by Retzius (figures 3–5). In recent years, knowledge of the nature and functions of spermatozoa has grown rapidly through the development of new methods of microscopy (ultraviolet, electron, phase-contrast, interference-contrast, and fluorescence), of histochemistry, and of experimental biology in general.

MORPHOLOGY AND PHYSIOLOGY

The function of the spermatozoon is to initiate the development of the egg and to supply the paternal hereditary material, and perhaps other important or essential components, to the new embryo. In order to achieve this the spermatozoon must, of course, first reach and enter the egg. With so formidable a task to perform it is not surprising that the spermatozoon is a complex and highly specialized cell. It arises in the tubules of the testis, from a spermatozoon mother cell, as the result of a process of cell division and differentiation, during which the chromosome number characteristic of the species is reduced by half.

The mature spermatozoon is a small, very

condensed cell made up of two major parts, the head and the tail. Its refractive index suggests that only about 50 per cent of it is water [3] (by contrast, water constitutes 80–90 per cent of most cells). The volume of the bull spermatozoon is only about one twenty-thousandth of that of the egg, to which it is equivalent in hereditary significance. Unlike eggs, spermatozoa are produced in prodigious numbers: an average ejaculate of bull semen contains about five thousand million spermatozoa, which is sufficient to inseminate successfully at least 500 cows.

The nucleus. The principal component of the head is the nucleus (figures 51 and 52). This is composed of densely packed chromatin which is extremely difficult to disintegrate by physical means; it gives the characteristic staining reactions for deoxyribonucleic acid (DNA) and strongly absorbs ultraviolet radiation (figures 36–41). In bull spermatozoa about 43 per cent of the chromatin is DNA [16]. The remaining 57 per cent is protein, of which half is said to consist of the amino acid arginine. The DNA present in the spermatozoon nucleus is equal in amount to half that of a normal somatic nucleus of the species concerned, and it is now believed that the genetic information carried by the spermatozoon is in some way stored in the structure of the DNA molecules. The chromatin appears to be more densely aggregated in the posterior part of the nucleus, but is otherwise homogeneous in distribution: even electron microscopy of very thin sections (0·02 μ) of spermatozoon nuclei has so far failed to reveal the presence of chromosomes.

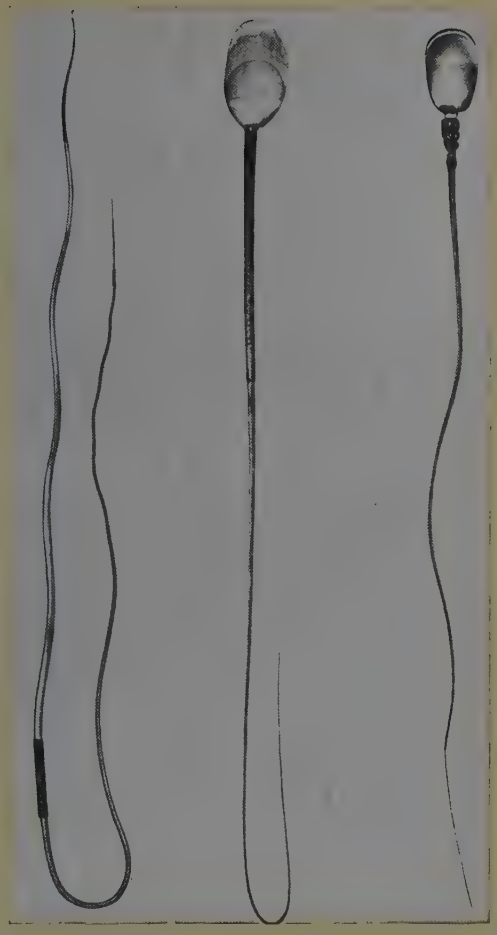
In mammals the hereditary properties of the spermatozoon nucleus include the determination of the sex of the embryo. The X- and Y-chromosomes, which occur together in the somatic cells of male mammals, are separated during the development of the spermatozoon and two kinds of spermatozoa are formed: those that carry the X-chromosome initiate the development of female embryos, and those that carry the Y-chromosome initiate the development of male embryos. Many attempts have been made to identify X and Y spermatozoa by measurement of nuclear size and to separate them by physical and chemical means, but it is doubtful whether any success has ever been achieved. Attempts have also been made to destroy the chromatin of spermatozoa by X-irradiation or chemical treatment while leaving the spermatozoon otherwise unimpaired. Such spermatozoa might be capable of initiating the development of embryos even though they transmit no active genetic material. Embryos produced in this manner would be females, but although the method is effective in certain amphibia it has not so far been successful in mammals.

In the spermatozoa of some rodents a slender process, the rod, extends from the nucleus to the apex of the hook-shaped head (figures 48 and 52). The rod, which contains no DNA, appears to be a thickened extension of the nuclear membrane [10]. It may function as a supporting structure for the acrosome (see below), but it is not found in the spermatozoa of microtine rodents [13], such as the field vole, which also have hook-shaped heads, and its significance is not clear.

The acrosome. The final stages of spermatogenesis involve the differentiation of the spermatid into the spermatozoon. During this process the Golgi apparatus of the spermatid is concerned with the formation of a cap-like structure, the acrosome, over the anterior surface of the nucleus. In mature spermatozoa the acrosome varies greatly in size and shape between different species, but its universal occurrence on the leading surface of the cell has for many years suggested that it plays a vital role in the penetration of the barriers that surround the egg. Many early workers believed that the acrosome had the function of mechanically piercing the egg membranes, and the sickle-shaped heads of some rodent spermatozoa lent themselves well to this interpretation. The hypothesis of simple mechanical function has, however, been long since rejected, and the acrosome is now regarded as probably providing a surface that is capable of attachment to the egg and of yielding enzymes that enable the spermatozoon to enter the egg. Evidence for these processes is still incomplete in mammals, but analogous functions of the acrosome have been demonstrated in the spermatozoa of certain invertebrates [11]. One indication that the mammalian acrosome plays a vital role in conception is that bull spermatozoa with an hereditary deformity of this structure (figure 55), but otherwise normal, are completely sterile [14].

From various lines of evidence, but particularly from studies of spermatogenesis, it seems that the acrosome is a double structure consisting of inner and outer caps (figures 51, 52, and 54). The two caps differ slightly in their staining reactions, but both give a positive reaction with the periodic acid Schiff (PAS) technique (figure 49) and for this reason are presumed to contain polysaccharide, possibly in the form of mucopolysaccharide. The acrosome also reacts characteristically with

FIGURE 1 (*Above, left*) – *Pouchet's picture* (*retouched*) *of the human spermatozoon. The head was believed to contain a simple alimentary tract.* (*From* Théorie positive de l'ovulation spontanée, et de la fécondation des mammifères et de l'espèce humaine, *Paris.* 1847.)



FIGURES 3–5 – *Retzius' pictures* (1906 *and* 1909) *of the spermatozoa of the Australian spiny ant-eater, the common European mole, and the pilot whale respectively.* (Biol. Untersuch., *N.F.*, **13** *and* **14**.)

FIGURE 2 (*Above, right*) – *Human spermatozoon as conceived by Hartsoeker, showing an homunculus seated in the head. The spermatozoon tail was thought to contain the umbilical cord.* (*From* Essay de dioptrique, *Paris.* 1694.)

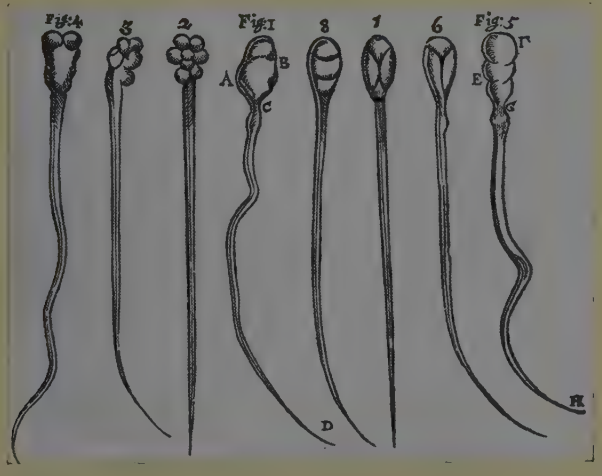


FIGURE 6 – *Spermatozoa of the rabbit* (*Nos.* 1–4) *and dog* (*Nos.* 5–8), *as portrayed by Leeuwenhoek.* (Phil. Trans., **12**, 1040, 1679.)

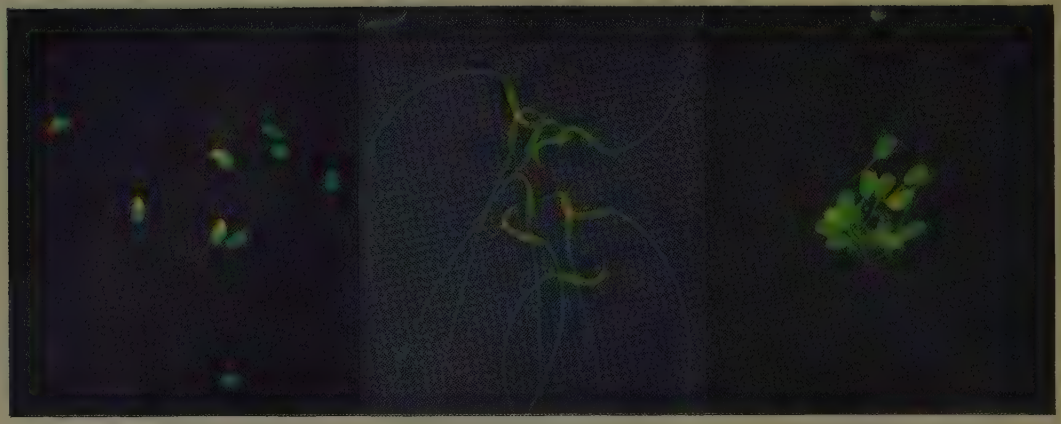


FIGURE 7 – *Cotton rat.* FIGURE 8 – *Albino rat.* FIGURE 9 – *Rabbit.*

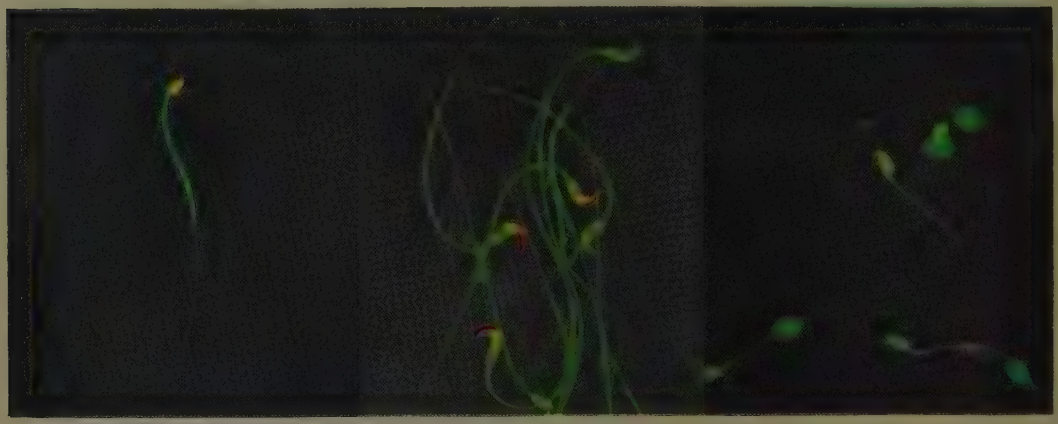


FIGURE 10 – *Libyan jird.* FIGURE 11 – *Golden hamster.* FIGURE 12 – *Field vole.*

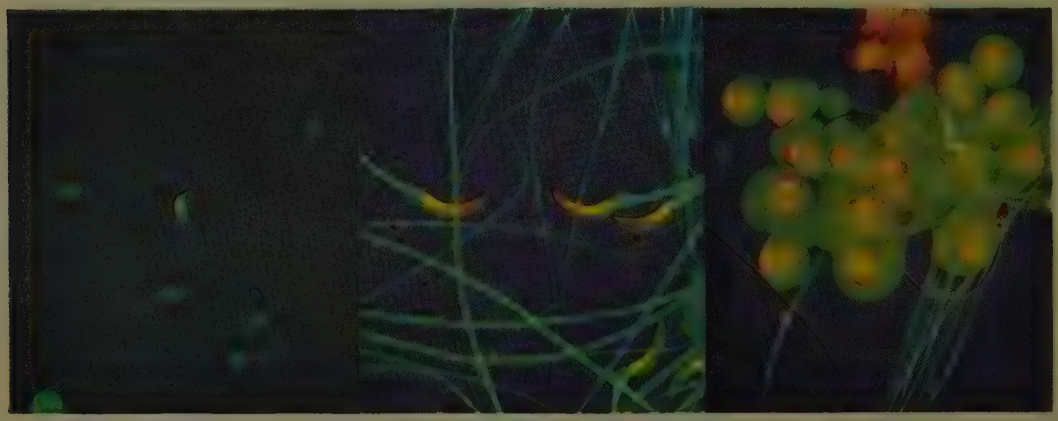


FIGURE 13 – *House mouse.* FIGURE 14 – *Chinese hamster.* FIGURE 15 – *Chinese hamster spermatids.*

FIGURES 7–15 – *Living mammalian spermatozoa and spermatids treated with acridine orange and photographed in ultra-violet radiation.* (× 660)

Giemsa's stain, often displaying a segment of lighter colour posteriorly (figures 42–45). This is called the equatorial segment, and is believed to represent the region in which the outer acrosome cap overlaps the inner one [15]. The posterior border of the outer acrosome cap also corresponds to the anterior border of the post-nuclear cap, a cytoplasmic sheath covering the posterior part of the nuclear surface which can be demonstrated by its argentophil properties (figures 46 and 47).

Recent developments in fluorescence microscopy have greatly facilitated the study of the acrosome in living spermatozoa [7]. The technique is simple: the spermatozoa are treated with a low concentration of acridine orange and then examined in ultraviolet radiation. Under these conditions the acrosomes of fresh, living spermatozoa are seen as brilliant red fluorescent images where they extend beyond the nucleus, and as yellow or yellowish-green images where they overlap the nucleus (figures 7–14 and 16). The nuclei, where not covered by the acrosome, appear bright green. The method gives spectacular results with rodent spermatozoa, especially those with large acrosomes, but is less successful with rabbit and bull spermatozoa, in which the acrosome is rather small. The significance of the polychromatic fluorescence obtained is not yet established, but recent work in which similar techniques have been used on other kinds of tissue has shown that structures containing DNA fluoresce green with acridine orange, while those containing ribonucleic acid (RNA) fluoresce red [1, 4]. It is, however, very unlikely that the acrosome contains appreciable amounts of RNA, for it cannot be stained with pyronine [12] and shows negligible absorption of ultraviolet radiation (figures 36–41). Furthermore, chemical analysis of mature spermatozoa reveals that they are remarkable for their lack of RNA [5], a deficiency that might be expected to limit their synthetic abilities. One property of the material responsible for the red fluorescence of the acrosome is, however, fairly clear. This is the ease with which it leaves spermatozoa that are washed, dried, or stored *in vitro* at room temperature (compare figures 16 and 17). Loss of this material may explain the variable results often obtained with more conventional methods of differentiating the acrosome. Ability of the acrosome to exhibit red fluorescence is also lost in the female genital tract; this occurs before the death of the spermatozoon and may be associated with loss of fertility.

Whereas the spermatozoon as a whole is remarkably resistant to distortion and disintegration, the acrosome is a relatively fragile structure and quickly shows degenerative changes when subjected to unfavourable conditions. These changes have often misled investigators in their interpretation of normal structure.

The tail and motility. The tail is the propulsive unit of the spermatozoon and pushes the cell along by the propagation of two-dimensional waves of bending, which pass distally along its length. It is a long (40–250 μ) flagellum, differentiated into four regions, the neck, the mid-piece, the main-piece, and the end-piece. During development, the rudiment of the tail arises as a slender filament from the spermatid centrioles and even at a very early stage exhibits undulating movements that appear to be initiated from the centrioles.

The neck is the short anterior extremity of the tail; very little is known of its detailed structure. Attached to the neck, but apparently embedded in the base of the nucleus, are the basal granules. By some techniques three granules are demonstrable in this region (figure 44), by others only two (figure 50). Possible explanations are that there are in fact three granules, of which two differ in their properties from the third, or else that the number differs in different species. Fluorescence microscopy with rhodamin shows two granules in the base of the head of motile rodent spermatozoa, but when the spermatozoa lose their motility the granules fail to fluoresce [7].

An axial core of twenty discrete fibres runs from the neck throughout the tail. The existence of such fibres has been known for almost 70 years, but their number and precise disposition within the tail have only recently been revealed by electron microscopy. It is now known that the axial core consists of two central fibres surrounded by nine fibres of similar diameter. These in turn are surrounded by a further ring of nine thicker fibres (figures 56 and 58) [9]. Available evidence indicates that the fibres pass straight along the tail and are not twisted about its axis. They appear to be gathered into three, or perhaps only two, bundles in the neck.

The mid-piece is characterized by a double mitochondrial helix surrounding the axial core. This helix can just be resolved by ultraviolet microscopy and is clearly demonstrable by electron microscopy (figure 57). It is formed by aggregation of mitochondria from the spermatid.

The main-piece is the longest part of the tail and provides most of the propellent machinery. Here the axial core is surrounded by a tough

helical protein sheath, down either side of which runs a small rib [9]. It bears no mitochondria.

The tail ends in a short (3–10 μ) distal endpiece, which is not surrounded by a helical sheath.

The possible mechanism by which the tail produces its characteristic movement has recently been discussed by J. R. G. Bradfield [9]. By virtue of their size and position, the nine fibres of the outer ring are thought to be the main contractile elements and to be capable of propagating localized contractions along their length. The helical protein sheath, together with an inter-fibre matrix, probably provide the skeletal structure against which the contractile fibres can work. The inner fibres may be specialized for the rapid conduction of impulses, arising rhythmically in the neck, which co-ordinate the localized contractions in the outer fibres. It may be noted in passing, however, that a simpler explanation could be advanced if the fibres were twisted about the axis of the tail instead of running straight as is at present believed. There is no evidence of contractile apparatus in the mitochondria, and it is likely that they are concerned solely with the provision of energy. Indeed, in view of the known localization of enzyme systems within mitochondria, and the role that these organellae play in the formation of high-energy phosphate compounds, the mid-piece is regarded as the main power house of the spermatozoon, though glycolytic enzymes may be distributed throughout the inter-fibre matrix. It is known that the tail contains all the apparatus necessary for motility, for tails that have been separated from heads can be fully motile.

Spermatozoa remain quiescent while within the epididymis but become actively motile at ejaculation (or when removed from the epididymis). The principal activating factor appears to be the increased availability of oxygen. The translatory speed of movement *in vitro* varies with the nature of the medium and with temperature, and is of the order of 100 μ per second at body temperature. Spermatozoa tend to orientate themselves against a current, for this is their position of greatest mechanical stability. On the other hand, there is no evidence that the direction of swimming is influenced by chemical gradients, and this suggests that the approach of the mammalian spermatozoon to the egg is not aided by chemotaxis.

One might suppose that the purpose of motility was to enable the spermatozoon to ascend the female genital tract to the site of fertilization in the Fallopian tubes, but this does not appear to be so, for in several species it is known that spermatozoa reach this site much more rapidly than they could by their own motility. Transport through the tract is almost certainly attributable to the muscular contractions of the walls of the tract and to currents produced by cilia that line these walls. The major function of motility, therefore, seems to be to assist the spermatozoon to penetrate the barriers surrounding the egg.

The cytoplasmic droplet. Most of the spermatid cytoplasm is eliminated from the cell during spermatogenesis, but a small bead, the cytoplasmic droplet, remains for a while attached to the neck of the spermatozoon. While passing through the epididymis the droplet migrates from the neck to the distal end of the mid-piece, and at the same time the spermatozoon develops its potentiality for motility and fertility. At ejaculation the droplet usually becomes detached.

The function of the cytoplasmic droplet remains one of the chief enigmas in the story of the spermatozoon. Its invariable presence on spermatozoa when released from the testis, its characteristic size and shape, and its ordered migration along the mid-piece signify that it is not merely a casual remnant of unwanted material. Its loss from the spermatozoon at the time of ejaculation, however, shows that its function must be concerned solely with the physiology of the spermatozoon within the male tract. This suggests that it may be involved in maturation processes or in the maintenance of the cell in a quiescent state and for a very much longer period than can be achieved at a similar temperature outside the epididymis.

The surface membrane. The surface membrane of the spermatozoon is composed of a lipid-protein complex, and phospholipids can be easily removed from it by washing in saline. The surface of the head, or perhaps only the part that is covered by the acrosome, is serologically distinct from the surface of the tail, and this difference is probably significant in fertilization. When the cell dies, the permeability of the membrane becomes greatly increased, and advantage has been taken of this to devise staining techniques that will distinguish living spermatozoa from dead ones (figure 18). The surface of the dead cell also has a high affinity for glass, and living spermatozoa can readily be separated from dead ones by filtration through a bed of fine glass beads [2].

Species differences in size and shape. Although mammalian spermatozoa are all constructed on a common pattern, the spermatozoa of each species display differences of shape and proportion that are quite characteristic. It is possible, indeed, to

Figure 16

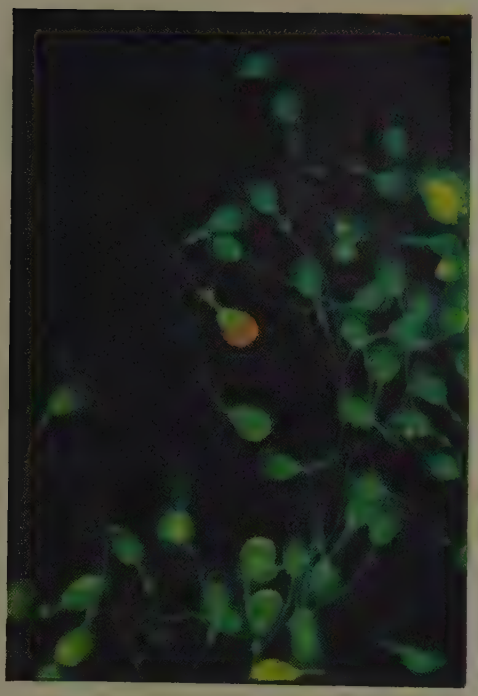


Figure 17

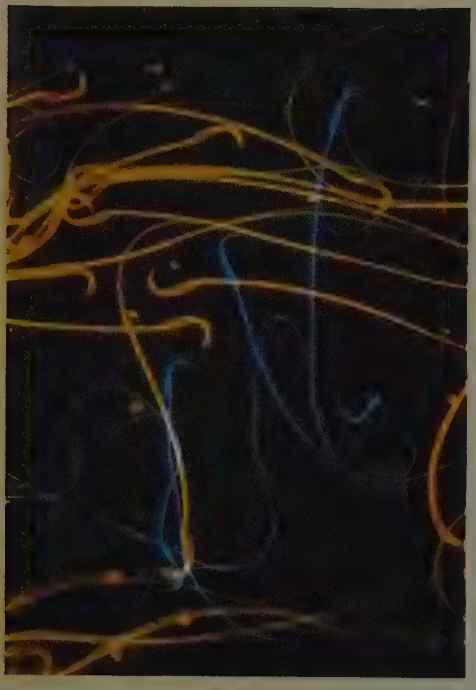


Figure 18

Figure 19

FIGURES 16 AND 17 – *Guinea-pig spermatozoa fluorescing in ultraviolet radiation after treatment with acridine orange. Those shown in figure* 16 *were photographed soon after collection; those in figure* 17 *had previously been kept for some time* in vitro. (× 660)

FIGURE 18 – *The different fluorescence exhibited by living (yellow) and dead (blue) rat spermatozoa when treated with a mixture of primulin and rhodamin B and examined in ultraviolet radiation.* (× 660)

FIGURE 19 – *Spermatozoa of the golden hamster treated with rhodamin* 6G *and examined in ultraviolet radiation. The fluorescent bodies at the base of the heads are interpreted as being the basal granules.* (× 660)

FIGURE 20 – *Tiger cat.* FIGURE 21 – *Long-nosed bandicoot.* FIGURE 22 – *Greater horseshoe bat.* FIGURE 23 – *Field vole.*

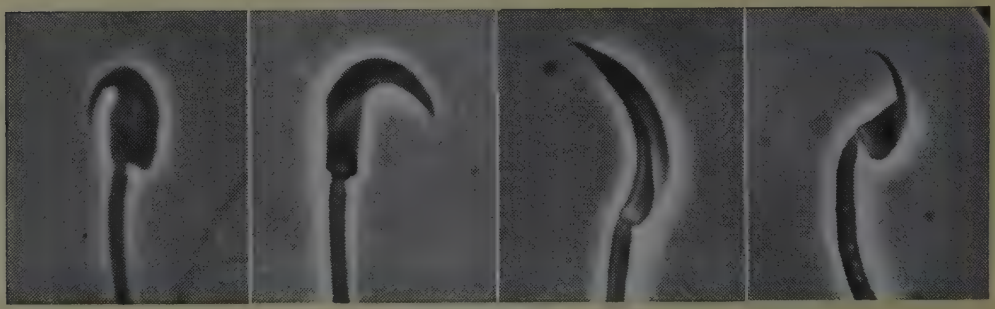


FIGURE 24 – *Cotton rat.* FIGURE 25 – *Golden hamster.* FIGURE 26 – *Chinese hamster.* FIGURE 27 – *Libyan jird.*

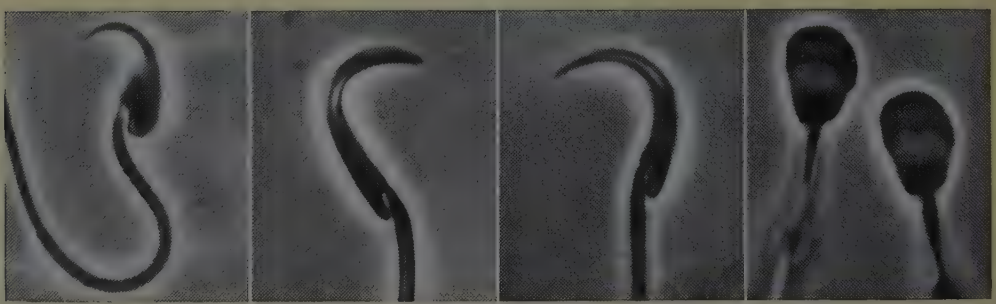


FIGURE 28 – *Barbary striped mouse.* FIGURE 29 – *Albino rat.* FIGURE 30 – *Multimammate rat.* FIGURE 31 – *Ferret.*

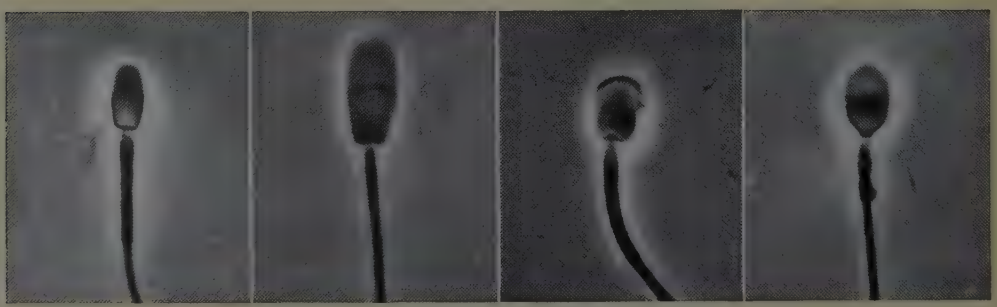


FIGURE 32 – *Cat.* FIGURE 33 – *Goat.* FIGURE 34 – *Greater bush-baby.* FIGURE 35 – *Man.*

FIGURES 20–35 – *The heads of living mammalian spermatozoa as seen by phase-contrast microscopy.* (× 2000)

FIGURE 36 – *Cotton rat.*

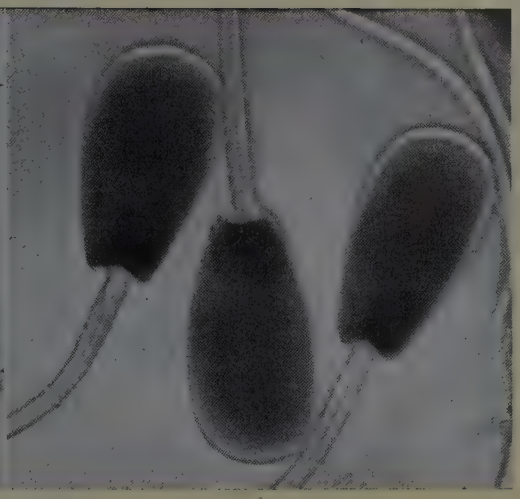


FIGURE 37 – *Bull.*

FIGURE 38 – *Greater horseshoe bat.*

FIGURE 39 – *Golden hamster.*

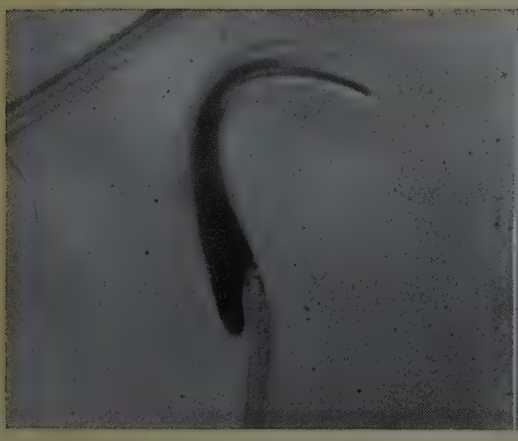


FIGURE 40 – *Albino rat.*

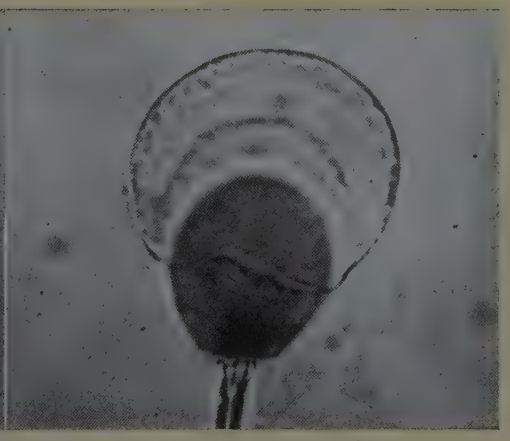


FIGURE 41 – *Guinea-pig.*

FIGURES 36–41 – *Ultraviolet photomicrographs of the heads of living mammalian spermatozoa, showing the strong absorption of radiation by the nucleic acid in the nucleus.* (× 4000 *approx.*) (*Figure* 37 *from* J. exp. Biol., **29**, 445, 1952.)

FIGURE 42 – *Golden hamster* (*Giemsa;* × 2900).

FIGURE 43 – *Boar* (*Giemsa;* × 2800).

FIGURE 44 – *Bull* (*Giemsa;* × 2400).

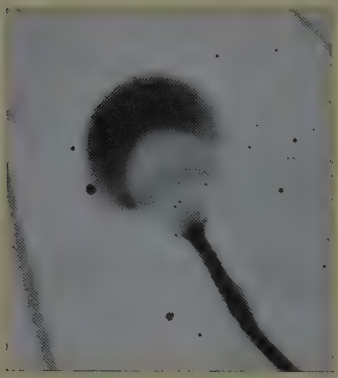


FIGURE 45 – *Guinea-pig* (*Giemsa;* × 2200).

FIGURE 46 – *Guinea-pig* (*silver impregnation;* × 2200).

FIGURE 47 – *Bull* (*silver impregnation;* × 2400).

FIGURE 48 – *Cotton rat* (*primulin;* × 1400).

FIGURE 49 – *Boar* (*PAS;* × 2800).

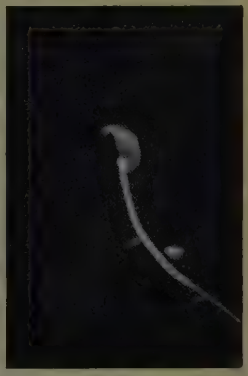


FIGURE 50 – *House mouse* (*rhodamin 6G;* × 1200).

FIGURES 42–50 – *Photomicrographs of stained preparations of mammalian spermatozoa, demonstrating the acrosome, the rod, the equatorial segment, the post-nuclear cap, and the basal granules.* (*Figure* 49 *in press,* J. R. micr. Soc.)

identify an animal merely by examining its spermatozoa. The overall size of the cell, though characteristic for each species, does not vary very greatly between species and is quite unrelated to the size of the animal concerned, but interspecific differences in the sizes of head and mid-piece relative to the whole spermatozoon are particularly notable. The projected area of the head of the guinea-pig spermatozoon, for instance, is nearly five times larger than that of the human, though the length of the guinea-pig spermatozoon is only about twice as great as the human. The mid-piece of the rat spermatozoon constitutes about 40 per cent of the total length of the tail, while that of the human spermatozoon amounts to no more than 10 per cent (compare also figures 4 and 5). Even more striking are the differences in the shape of the head. In most large animals the head is a more or less oval and flattened structure. In man (figure 35) it is oval in plan view but pear-shaped in sagittal section. In many rodents (figures 23–30) it is asymmetrical and often hook-shaped. In many marsupials the head is deeply invaginated at the posterior end (figure 21), but in some it is more rod-like in form (figure 20); the head appears to be pivoted at the point of insertion of the neck. The spermatozoa of the egg-laying monotremes (figure 3) have long, narrow vermiform heads and resemble the spermatozoa of birds more than those of mammals. It is not known whether there is any adaptive significance in the differences of shape between species. Differences of head shape between strains within a species have also been demonstrated for spermatozoa of the mouse [8].

Metabolism and survival. It was formerly believed that mammalian spermatozoa were incapable of utilizing extracellular nutrient and that the limit of their independent existence was determined by the intracellular food reserves acquired during spermatogenesis. It is now well known, however, that these cells can metabolize a number of extracellular substrates and use the energy so obtained to maintain their physiological functions. Chief of the energy-providing systems available to mammalian spermatozoa are the Embden-Meyerhof glycolytic system, by which fructose and glucose can be broken down to lactic acid, and the cytochrome oxidase-cytochrome system and Krebs cycle, by which a variety of substrates, but notably lactate and pyruvate, can be oxidized to carbon dioxide and water. Even in the absence of exogenous substrate, mammalian spermatozoa can respire actively and maintain their motility for an appreciable time. Under these conditions it is believed that they obtain energy by the oxidation of endogenous phospholipid, a characteristic component of mitochondria, in a manner closely analogous to the normal metabolism of sea-urchin spermatozoa [19]. It is believed that the oxidative enzymes are all located within the mitochondria, but the Embden-Meyerhof enzymes are generally regarded as being cytoplasmic in distribution and are therefore probably more widely spread throughout the cell. Glycolytic metabolism can take place under anaerobic conditions, but yields much less energy than aerobic oxidation.

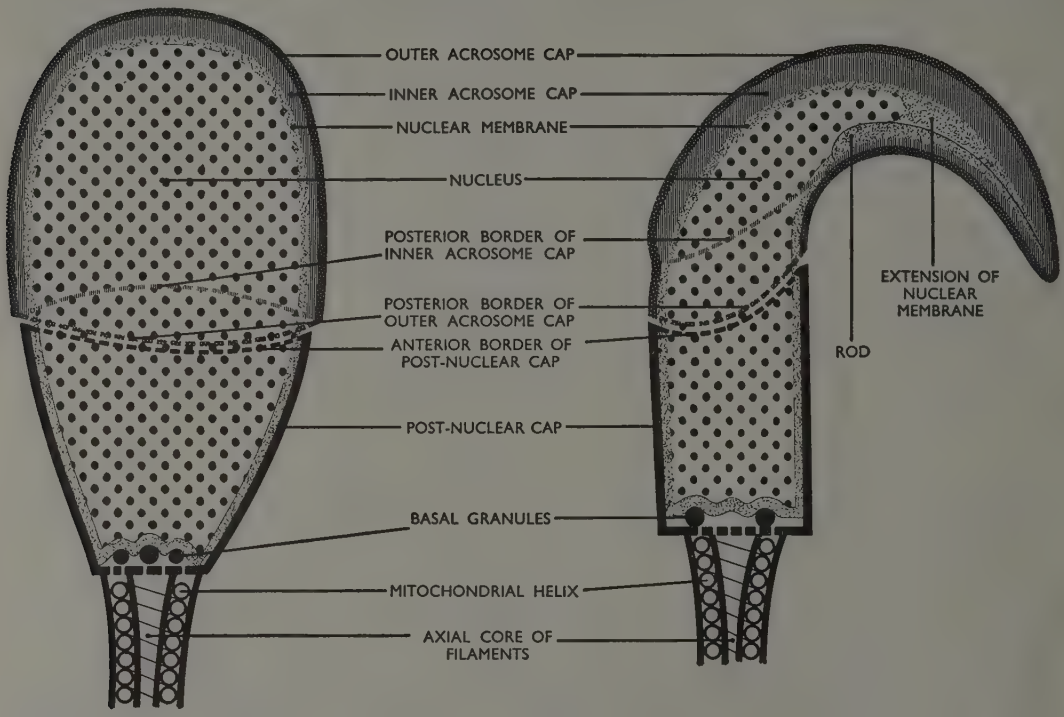
Metabolism is not, however, restricted to catabolic processes. Recent work shows that mammalian spermatozoa synthesize lipids [17] and incorporate amino acids into their proteins [5]. The incorporation of amino acids is of special interest in view of the apparent absence of RNA from spermatozoa.

It seems likely that aerobic oxidation plays the dominant role in spermatozoon metabolism within the female reproductive tract, because both oxygen and lactate are available in this situation. In most species, however, spermatozoa do not survive for more than one or two days within the female tract, though some bats provide notable exceptions to this. Within the epididymis, spermatozoa appear to exist under conditions in which both oxygen and glycolysable sugar are deficient; nothing is known of their metabolism in this location, but metabolic activity is probably low. Here they retain their fertility for one or two months and their potential for motility for rather longer. They survive for only a short time *in vitro* at body and room temperatures, but survival time can be prolonged by reducing the temperature of storage. By dilution with suitable media and careful cooling, the fertility of bull spermatozoa can be preserved for several days at 4° C and for years at −79° C [18].

THE SPERMATOZOON IN FERTILIZATION

In order to enter the egg the spermatozoon must pass through three barriers. These are the thin vitelline membrane which encloses the protoplasm of the egg proper; the thick (10–12 μ) mucoproteinous zona pellucida; and several layers of follicle cells which adhere to the zona pellucida and are embedded in a gelatinous matrix composed largely of hyaluronic acid.

Spermatozoa pass between the layers of follicle cells, traversing the matrix with the aid of hyaluronidase, an enzyme that can be very easily

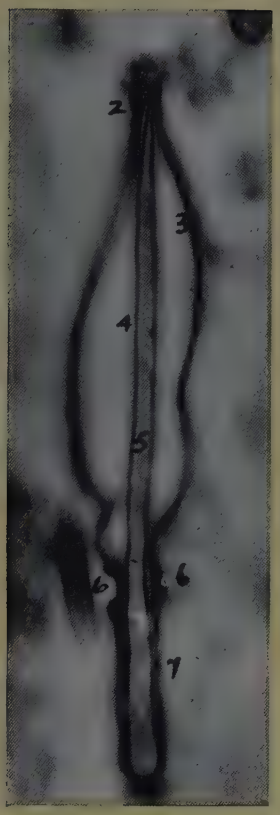


FIGURES 51 AND 52 – *Diagrammatic representation of the probable structure of the heads of bull (left) and hamster (right) spermatozoa respectively.*

extracted from mammalian spermatozoa. In the presence of large numbers of spermatozoa the follicle cells are quickly dispersed from the egg, but despite the hundreds of millions of spermatozoa that are released into the female tract at coitus only a few thousand attain the site of fertilization, and those that first reach the eggs are too few to denude them. Penetration of the egg occurs before dispersal of the follicle cells, which may in fact assist entry of the spermatozoon by increasing the target area, and by guiding spermatozoa toward the egg. Evidently the hyaluronidase associated with the individual spermatozoon is sufficient to enable it to make its way through the mass of follicle cells. It seems likely that the spermatozoon hyaluronidase is carried by the acrosome: it may in fact be associated with the labile material that exhibits a red fluorescence after treatment with acridine orange.

On reaching the zona pellucida, the spermatozoon becomes attached to its surface by the acrosome, and there is evidence that this attachment is made by an antigen-antibody type of reaction [6]. The spermatozoon then proceeds to penetrate the zona pellucida, presumably with the aid of another enzyme also located within the acrosome. Attempts to extract this enzyme from mammalian spermatozoa have so far failed, but a small hole that remains in the zona pellucida after the passage of the spermatozoon testifies to its probable existence. A remarkable feature of this penetration, however, is that it cannot take place until the spermatozoa have remained for a short period within the female tract and have undergone some kind of preparatory change. The change is called capacitation; its nature is unknown, but is supposed to involve activation of the hypothetical enzyme within the acrosome. The need for capacitation probably explains the present failure to extract an active zona-pellucida lysin from spermatozoa and the difficulty of fertilizing mammalian eggs *in vitro*.

After penetrating the zona, the spermatozoon becomes attached to the vitelline membrane, and is then apparently slowly engulfed by the cytoplasmic part of the egg. First the spermatozoon head, and then the tail, sink slowly into the egg cytoplasm. This entry is associated with the stimulation of the egg to development and with changes in the vitelline membrane and the zona



FIGURES 53 AND 54 – *Longitudinal sections of heads of boar and ram spermatozoa respectively.* 1, *outer acrosome cap.* 2 *and* 3, *inner acrosome cap.* 4, *nuclear membrane.* 5, *nucleus.* 6, *junction of acrosome and post-nuclear cap.* 7, *post-nuclear cap. The separation between the acrosome and nucleus in figure* 53 *is an artefact.* (× 13 000 *and* × 38 000 *respectively.*)

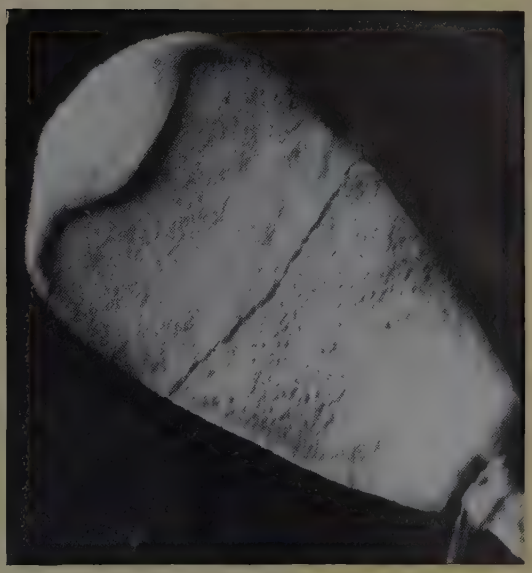


FIGURE 55 – *Head of bull spermatozoon, showing an hereditary defect of the acrosome (gold-palladium shadowed;* × 9000).

FIGURE 56 (*Right*) – *Transverse section of the mid-piece of the tail of a ram spermatozoon.* (× 60 000)

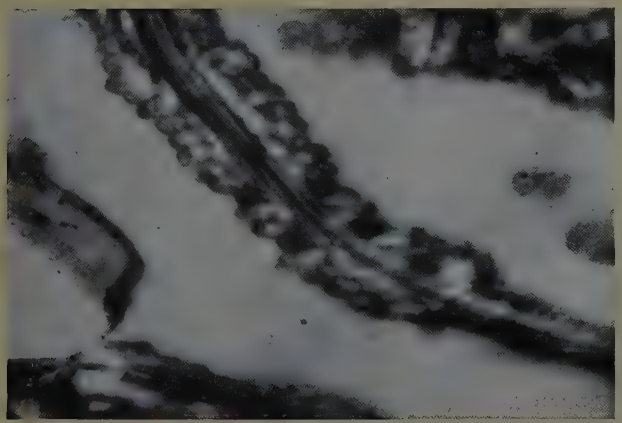


FIGURE 57 – *Longitudinal section of part of the mid-piece and main-piece of the tail of a ram spermatozoon, showing the mitochondrial helix and the axial filaments.* (× 20 000)

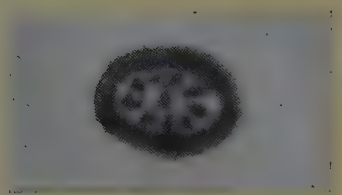


FIGURE 58 – *Transverse section of the main-piece of the tail of a boar spermatozoon. The inner and outer rings of nine fibres and the two central fibres are not separately resolved in this photograph.* (× 50 000)

FIGURES 53–58 – *Electron micrographs of boar, bull, and ram spermatozoa.* (*Figure* 55 [14]; *figure* 56 [9].)

pellucida that render these membranes impenetrable to further spermatozoa. The membrane changes reduce the danger of fertilization by more than one spermatozoon, an event that seems to be incompatible with survival of the resulting embyro.

Inside the egg the spermatozoon nucleus increases greatly in size and loses its characteristic shape. The nucleus then moves towards the centre of the egg, as does a similar nucleus produced by the egg. The two nuclei come into close contact, the nuclear membranes disappear, and the nuclei are replaced by two chromosome groups, which come together to form a single group. This marks the end of fertilization and the beginning of the first cleavage mitosis of the new embryo. The union of the two haploid chromosome groups re-establishes the diploid number of the species. When the egg divides, each chromosome duplicates itself and each daughter cell receives an equal share of the chromosomes supplied by the spermatozoon and by the egg.

Since as a general rule the entire spermatozoon enters the egg, it is possible that spermatozoon structures other than the nucleus may play an important part in the development of the new embryo. It has been suggested that the acrosome is responsible for stimulating the egg to active development, that spermatozoon centrioles play an essential role in the formation of the first cleavage spindle, and that mitochondria from the midpiece remain functional within the egg cytoplasm. As yet, however, there is little evidence for these processes in mammals.

APPENDIX

LIST OF SPECIES OF WHICH THE SPERMATOZOA ARE ILLUSTRATED

	Figure
MONOTREMATA	
Australian spiny anteater, *Tachyglossus aculeatus*	3
MARSUPIALIA	
Tiger cat, *Dasyurops maculatus*	20
Long-nosed bandicoot, *Perameles nasuta*	21
PLACENTALIA	
Common European mole, *Talpa europaea*	4
Greater horseshoe bat, *Rhinolophus ferrum-equinum*	22, 38
Greater bush-baby, *Galago crassicordatus*	34
Man, *Homo sapiens*	35
Ferret, *Mustela furo*	31
Cat, *Felis catus*	32
Pilot whale, *Globicephalus melaena*	5
Boar, *Sus scrofa*	43, 49, 53, 58
Bull, *Bos taurus*	37, 44, 47, 51, 55
Ram, *Ovis aries*	54, 56, 57
Goat, *Capra hircus*	33
Rabbit, *Oryctolagus cuniculus*	9
Barbary striped mouse, *Lemniscomys barbarus*	28
Albino rat, *Rattus norvegicus*	8, 18, 29, 40
Multimammate rat, *Mastomys coucha*	30
House mouse, *Mus musculus*	13, 50
Golden hamster, *Mesocricetus auratus*	11, 19, 25, 39, 42, 52
Chinese hamster, *Cricetulus griseus*	14, 15, 26
Cotton rat, *Sigmodon hispidus*	7, 24, 36, 48
Libyan jird, *Meriones libycus*	10, 27
Field vole, *Microtus agrestis*	12, 23
Guinea-pig, *Cavia porcellus*	16, 17, 41, 45, 46

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We are indebted to Mr J. Smiles for his invaluable assistance with problems of microscopy, to Mr M. R. Young for his skill in obtaining the ultraviolet and fluorescence photomicrographs of figures 7–19 and 36–41, to Dr J. L. Hancock for supplying some of the photomicrographs of stained spermatozoa (figures 43, 44, 49), to Dr J. R. G. Bradfield for the electron micrographs (figures 53–58), and to Dr Adolph Bolliger, Professor E. C. Amoroso, and Mr Michael Blackmore for providing for study spermatozoa of marsupials, the cat, and the greater horseshoe bat respectively.

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Ferromagnetic domains

L. F. BATES

The physical processes involved when a ferromagnetic metal is magnetized have been the subject of much study. In this article are described some recent contributions to our knowledge of these processes that have been obtained by techniques which, though elaborate, are fundamentally no more than those familiar to every elementary student of magnetism and enable us to follow some of the processes in considerable detail.

INTRODUCTION

In this article will be described some interesting and important results obtained by a modern variant of the familiar experiment of plotting lines of magnetic force by means of iron filings. The striking magnetic properties of ferromagnetic substances like iron are currently attributed to special aligning forces, called exchange forces, between spinning electrons in neighbouring atoms. The main object of the present investigations is to obtain detailed information about what happens when a ferromagnetic substance is exposed to magnetizing influences, in order to test basic magnetic theories and to provide a logical basis for improving the performance of ferromagnetic materials. Since a polycrystalline material usually consists of a large number of very small crystals whose boundaries give rise to phenomena which, though very interesting, greatly complicate the experiments, most of the work has been confined to single-crystal specimens.

Let us first consider the magnetic behaviour of a single crystal of cobalt, as we have in this a very clear example of what is termed ferromagnetic crystalline anisotropy. The crystal may be represented as a hexagonal block, which at ordinary temperatures may be magnetized with ease in either of the two directions parallel to the axis of the block but only with some difficulty in any direction perpendicular to this, i.e. in the plane of the hexagon. Because of this property, the first two directions are called the directions of easy magnetization.

To account for the ease with which a demagnetized ferromagnetic metal may be magnetized almost to saturation by the application of a weak magnetic field, it is assumed that the metal consists of a very large number of elementary regions or domains, each magnetized to saturation, and the magnetic vector in each domain is considered to be parallel to a direction of easy magnetization in the crystal of which it forms a part. In the demagnetized specimen the magnetic vectors of the several domains must in general be randomly distributed or, in special cases, arranged in a closed configuration. Between domains there must then be a boundary or a narrow region of transition.

On the application of a magnetic field to a demagnetized crystal two main changes occur. Firstly, those domains whose magnetic vectors make an angle less than 90° with the applied field increase in size at the expense of their less favourably magnetized neighbours by what is termed boundary displacement. Secondly, the vectors of the individual domains tend to rotate in order to set as nearly as possible parallel to the field. The first change occurs mainly in low and moderate fields and the second in high fields, although they are frequently superimposed. In very strong fields all the vectors point along the field direction and the crystal is technically saturated, being in effect one large single domain.

EXPERIMENTAL TECHNIQUE

For such study a crystal must be carefully shaped and its surface properly prepared. It is usually given a good mechanical polish, and the amorphous, strained surface layer which results is later removed by electrolytic polishing in a special bath, using a simple bridge circuit [1] to control the current. Cobalt is one of the easiest metals to prepare for study in single-crystal form.

The polished surface is mounted horizontally, and upon it a drop of a colloidal solution of magnetite is placed or a very fine ferromagnetic powder is blown. The magnetite or powder particles form a pattern which may be viewed or photographed with a metallurgical microscope, using a magnification of between 50 and 400. Such patterns are known as powder patterns or Bitter figures [2]. The best results are normally obtained with colloidal magnetite solutions prepared according to W. C. Elmore's recipe [3, 4].

EXPERIMENTS WITH COBALT CRYSTALS

When we apply this technique to a strip from the face of a single crystal of cobalt cut parallel to the hexagonal axis, a pattern like that of figure 3 is obtained for the demagnetized state. The horizontal dark lines of colloid separate domains which are alternately magnetized along one or the other of the two directions of easy magnetization. The dagger-shaped figure in the right-hand portion of the picture is a closure domain, a subsidiary structure whose function is described below, and this is magnetized anti-parallel to the principal domain in which it lies. The serrated outline in the middle of the picture is very unusual, and is probably due to sub-surface damage to the crystal.

The heavy-line deposits occur because there is a 180° domain wall between two neighbouring domains. Now, ferromagnetism is attributed to exchange interaction between electron spins, and the electrons responsible for ferromagnetism in neighbouring domains must have their spin vectors aligned in opposite directions. Consequently, along a line of atoms running through the wall and perpendicular to it, the direction of electron spin must change continuously from atom to atom. This will be made manifest by an emergent stray field above the intersection of the domain wall with the crystal surface, and here magnetic dipoles in the colloid are attracted and attach themselves.

When a magnetic field is applied to the specimen shown in figure 3 in a direction parallel to the crystal axis, the specimen becomes magnetized by 180° boundary displacement. Alternate domains expand and contract sideways until the crystal becomes one large domain and all boundaries disappear. In figures 4 and 5 are seen the effects of applying a small magnetic field perpendicular to the surface. Since the surface is unlikely to be an exact crystal plane, it must have a small component of magnetization normal to the surface in each domain. This component will be either increased or decreased on the application of a weak perpendicular field. In figure 4 such a field runs into, and in figure 5 out of, the surface, and by using imperfections in the surface as reference points it is seen that the two patterns are reversed.

In the first photograph there are also to be seen many short black lines or vertical streaks of deposit running at right angles to main domain walls. They arise from accidental small depressions or troughs formed during polishing. When a trough runs perpendicular to the direction of magnetization of a domain, a stray field bridges the trough and colloid particles are attracted into it. When, however, a trough runs parallel to the direction of magnetization, a stray field does not traverse it and colloid is not deposited. By deliberately making very fine scratches on the surface with a glass fibre [5], tests can thus be made of the direction of domain magnetization. On the basal plane of the cobalt crystal, characteristic star patterns are formed, as shown in figure 6.

EXPERIMENTS WITH SILICON-IRON CRYSTALS

Most domain studies have been made with crystals of silicon-iron containing some 3 per cent silicon. In these body-centred cubic crystals there are six directions of easy magnetization, parallel to the cube edges. The patterns which may be observed on a cube face, or (100) surface, are particularly instructive. In the demagnetized state the surface is usually covered by a 'fir-tree' pattern, like that reproduced in figure 7; its formation is explained as follows [5]. The branches of the fir-trees are formed when the crystal surface departs slightly from a true (100) plane. The trunk of the fir-tree in figure 7 is formed by the intersection of a 180° wall with the surface. The branches, which are magnetized in directions perpendicular to those of the main domains, are formed by ellipsoidally shaped closure domains which run out from the domain walls within the crystal to give triangular intersections with the surface. The function of the closure domains is to reduce 'free' surface magnetism as much as possible. The more accurately the surface approximates to a true (100) plane the larger and fainter are the branches.

In figure 8, obtained when a weak magnetic field was applied parallel to the 180° domain wall which runs near the middle of the picture, the directions of magnetization in certain domains are marked with arrows. In the case of the fir-tree with its branches perpendicular to the trunk shown in the upper left quadrant of the picture, the trunk is formed by the intersection of a 90° domain wall with the surface; i.e. the wall separates two domains whose magnetic vectors are perpendicular to each other. As before, the branches are formed by the intersection of ellipsoidal closure domains with the surface, and in this instance the branches join the trunk in two different ways.

Below the centre of figure 8 there appears a structure like a tree with a wide trunk. This is a structure which is termed a domain of reverse magnetization. As the weak magnetic field is

increased, the wide trunk expands and the tree lengthens at an enormous rate, so that finally the whole surface is covered by the trunk and is one single domain.

QUANTITATIVE EXPERIMENTS

Interesting quantitative experiments have been made with specially cut and shaped crystals of silicon-iron. For example, H. J. Williams and W. Shockley [6] cut a section parallel to a cube face and then shaped it to form a kind of picture frame with its sides parallel to cube edges. In the unmagnetized state a single 180° domain wall was made to run in an unbroken manner completely round the surface of the frame, so that on the inner side of the wall the specimen was magnetized in a clockwise direction and on the outer side of the wall in an anticlockwise direction. By passing a current through a fine coil wound on one side of the frame the crystal could be exposed to a magnetizing field, whereupon the wall moved, and the changes in magnetization could be measured and correlated with the position of the boundary.

L. Néel [7] first drew attention to the remarkable behaviour of a thin specimen of iron cut as depicted in figure 1. The upper and lower surfaces are (100) planes and the sides are (110) planes, so that the long axis of the specimen is a [110] direction, i.e. a diagonal drawn on a cube face. When only a very small field acts parallel to this axis the state of affairs shown in figure 1(*a*) obtains; successive principal domains are alternately magnetized parallel to the [001] and [00$\bar{1}$] directions, the two directions of easy magnetization. A simple system of *q* closure domains serves to prevent 'free' surface magnetism on the sides. When an appreciable magnetic field *H* is applied, the principal domain vectors rotate inwards as in figure 1(*b*), and simultaneously a new set of *p* closure domains is established.

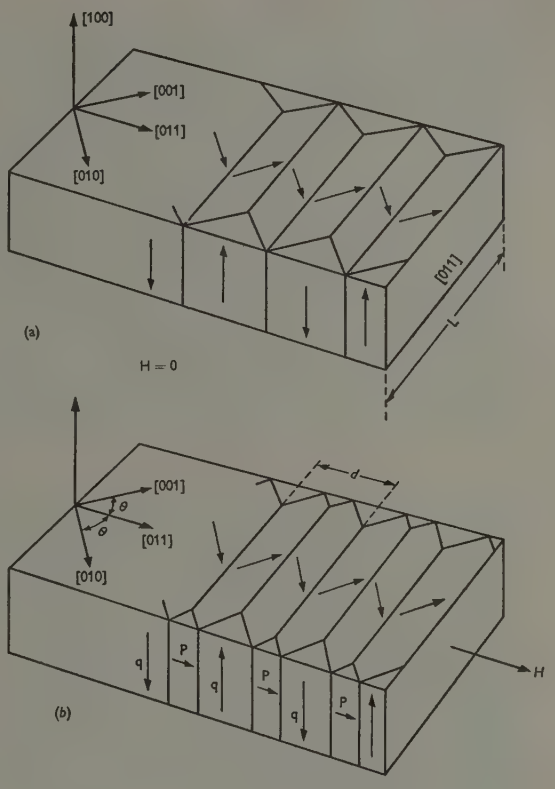

FIGURE 1 – *Domain structure of Néel-cut specimen.*

Specimens cut according to figure 1 have frequently been examined [5, 8–10], and a pattern is shown in figure 9. A dense colloid solution was here used to bring out the direction of magnetization in alternate domains; the strange circular patterns in the middle of the picture are probably due to defects below the surface. In such experiments the magnetic field obtained by placing the strip between the poles of a simple electromagnet is measured by a magnetic potentiometer [11], and the period *d* is measured from photographic records. In figure 2 a series of measured values of *d* are plotted against the corresponding values of the field *H*, together with the theoretical curve based on figure 1(*b*) [11]. There is undoubtedly numerical discrepancy between experiment and theory, but the general agreement is satisfactory. In any case exact agreement is not to be expected, because the patterns found on the (110) side surfaces, called lace patterns, are very complex. When the crystal is thick they are well defined, as in figure 12(*a*), with a period *d'* equal to that found on the (100) surface, although in some specimens [10, 12] they are inclined at an angle of as much as 15° to the expected direction; for this there is as yet no explanation. With narrow specimens, patterns like those of figure 12(*b*) are obtained. We have, in fact, definite evidence of 'free' surface magnetism, which is not envisaged in the theory.

THE EFFECTS OF IMPERFECTIONS

Néel was the first to point out that if there existed within a domain a defect, e.g. a tiny hole, an inclusion, or a small patch of strained material, a very large magnetostatic energy would be associated with it unless small closure domains were

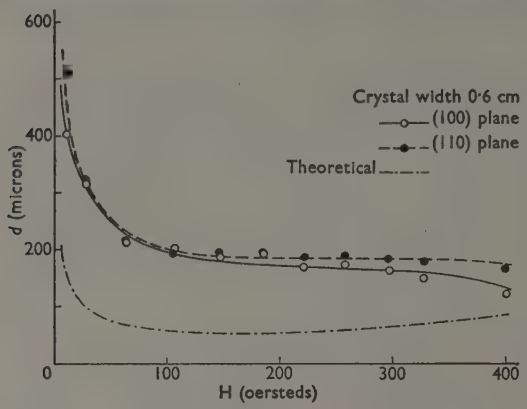

FIGURE 2 – *Variation with field of domain spacings on* (100) *and* (110) *planes.*

formed around it. Such systems were first photographed by the powder technique by Williams [13]. In figure 10 two closure systems are shown, one on either side of the 180° boundary which runs down the middle of the picture. Incidentally, this boundary is slightly waved, indicating the presence of many small defects, to which it is anchored. The closure systems are shaped somewhat like boomerangs, and they must be due to ellipsoidal-shaped structures, magnetized perpendicular to the main domain, giving triangular intersections with the surface.

Remarkable sequences of pictures were obtained by D. H. Martin [14] when 90° and 180° boundaries were caused to move across inclusions by the application of a magnetic field. But before similar pictures are described here it is helpful to discuss a phenomenon whose importance has only recently been appreciated [6, 15]. In figure 11 two 180° walls are seen. To the left of the wall nearest the middle of the picture is an inclusion on which is based a long Néel 'spike' closure domain, pointing upwards to the left. Between the two 180° walls is a somewhat deformed spike arising from another inclusion. But, in addition to the spikes, one notes that both inclusions are anchored to the 180° walls by tubes. It is now thought that such tubes play an important part in hysteresis phenomena. As a wall moves away from an inclusion, the tube reaches a critical length and then collapses to form a spike. In like manner, when a wall approaches a short spike, the latter elongates and attaches itself to the wall. This phenomenon is described as tube extension (*Schlauchziehen*); it is now being studied under controlled conditions.

During such a study P. M. Griffiths obtained the set of pictures shown in figures 13(*a–f*). In this can be followed the approach of a 180° wall towards a small pit formed in the surface during polishing, its sweep through the pit, and its eventual movement away from it. As the wall moves from right to left, we note the collapse of the tubes anchored to the wall, their almost complete disappearance when the wall intersects the pit, and their re-formation as the wall moves away from it. Finally, we see that one of the tubes, the upper in (*f*) has collapsed to form a spike. Figure 13(*c*) gives an excellent idea of a highly localized closure domain system formed when the plane of the wall intersects the inclusion. Such processes cannot be reversible, yet they must be common inside polycrystalline materials, and their formation and disappearance must be accompanied by micro-eddy current thermal changes [16].

It is pertinent to enquire what happens when a specimen is magnetized more or less to saturation in a strong field, so that it is effectively one large single domain, and the field is then slowly reduced to zero. Why should the single domain configuration not remain? Taking the simplest case, that of a (100) surface of silicon-iron magnetized to saturation along a cube edge, Martin [16] showed the extraordinary importance of inclusions, imperfections, and artificial defects. He showed that from such centres there arise domains of reverse magnetization, such as the one mentioned in describing figure 8. Once formed, these domains need only a small change of field to cause them to sweep across the whole surface.

NEW PATTERNS OF SPECIAL SIGNIFICANCE

In order to find to what extent the patterns found on polycrystalline surfaces resemble those on single crystal surfaces, A. Hart [17] made a special study of grain-orientated silicon-iron in which the planes of intersection of many of the grains in a sheet surface are close to a (110) plane. Patterns were observed which were virtually the lace patterns previously observed on the (110) surface of a Néel-cut specimen. In the course of this study some interesting 'tadpole' patterns were recorded. They always appeared near the edge of a grain, and it was therefore concluded that they were a special type of closure structure covering a more elementary domain structure, and that the heads of the tadpoles were evidence of highly localized stray fields. It is now considered that they are formed by the intersection of a large Néel

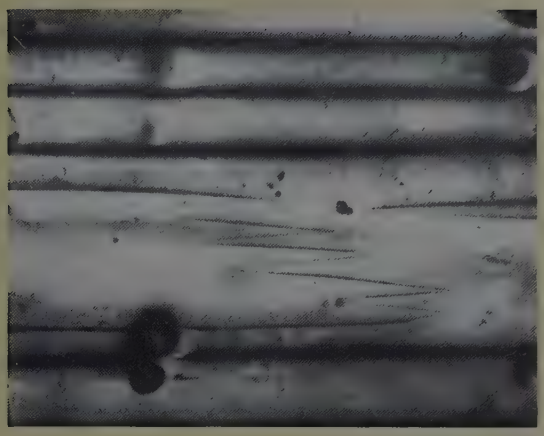

FIGURE 3 – *Powder patterns on the* (10$\bar{1}$0) *face of a single crystal of cobalt in the demagnetized state.* (× 110)

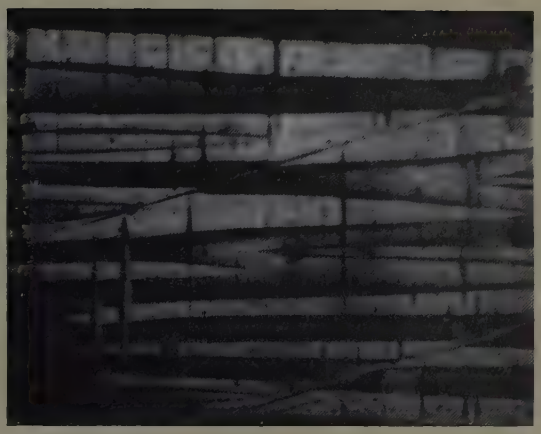

FIGURE 4 – *Cobalt. Demagnetized state,* (10$\bar{1}$0) *surface. Small normal field applied.* (× 125)

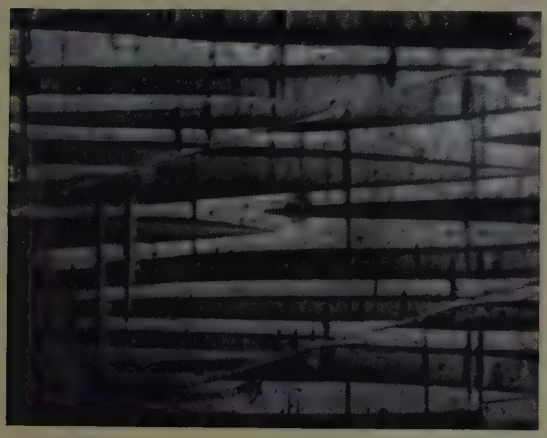

FIGURE 5 – *Cobalt. Demagnetized state,* (10$\bar{1}$0) *surface. Same as figure* 4 *but with field reversed.* (× 125)

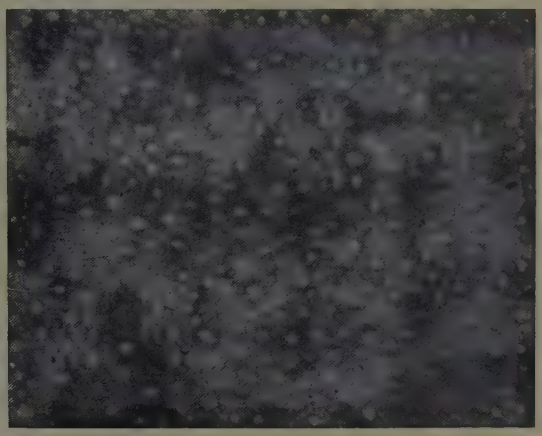

FIGURE 6 – *Powder pattern on the basal plane of a cobalt crystal in the demagnetized state.* (× 110)

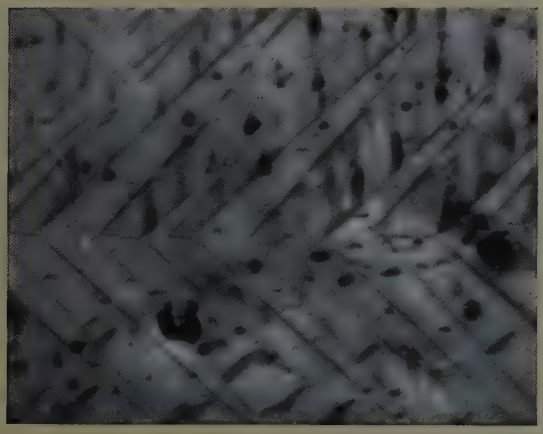

FIGURE 7 – '*Fir-tree*' *patterns on approximate* (100) *surface of silicon-iron in the demagnetized state.* (× 180)

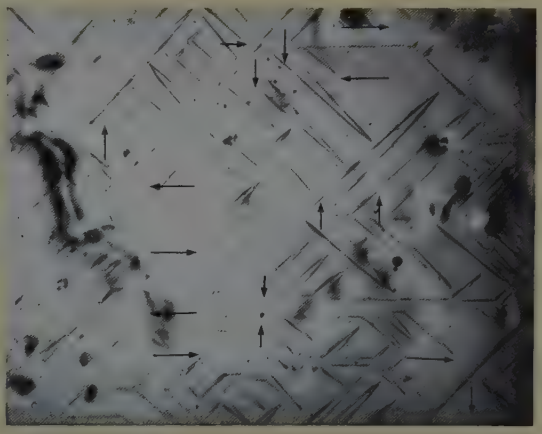

FIGURE 8 – '*Fir-trees*' *and a domain of reverse magnetization on approximate* (100) *surface of silicon-iron; a very weak field acts on the almost demagnetized crystal.* (× 80)

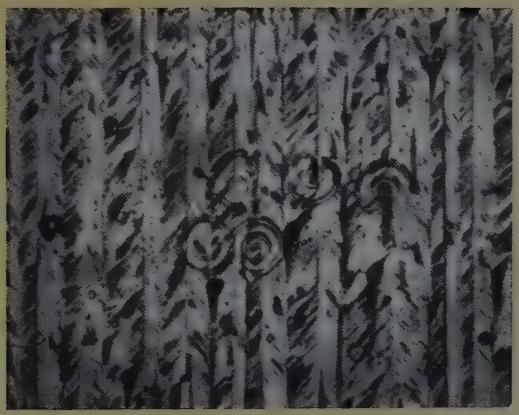

FIGURE 9 – *Lines on Néel-cut silicon-iron crystal. Field applied parallel to* [011] *direction, i.e. perpendicular to the lines of colloid.* (× 125)

FIGURE 10 – *Closure domain structures on a* (100) *surface of silicon-iron. A* 180° *boundary runs through the middle of the picture from top to bottom.* (× 200)

FIGURE 11 – *Néel spikes, and tubes attached to an inclusion and a* 180° *wall, on a* (100) *surface of silicon-iron.* (× 90)

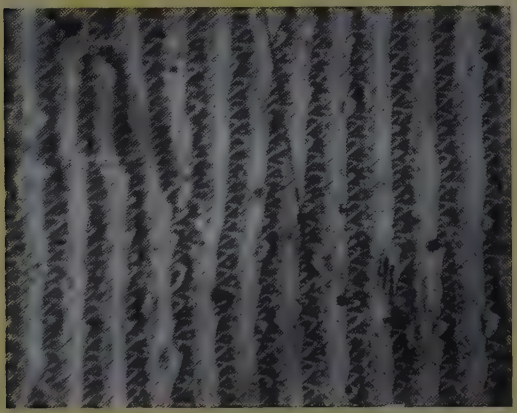

FIGURE 12(*a*) – *Lace patterns on* (110) *surface of silicon-iron.* (× 115)

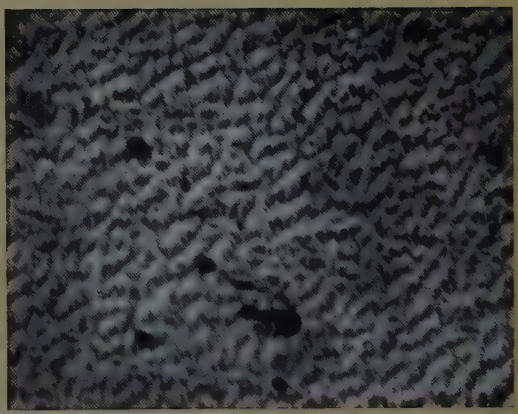

FIGURE 12(*b*) – *Lace patterns on* (110) *surface of thin specimen of silicon-iron.* (× 125)

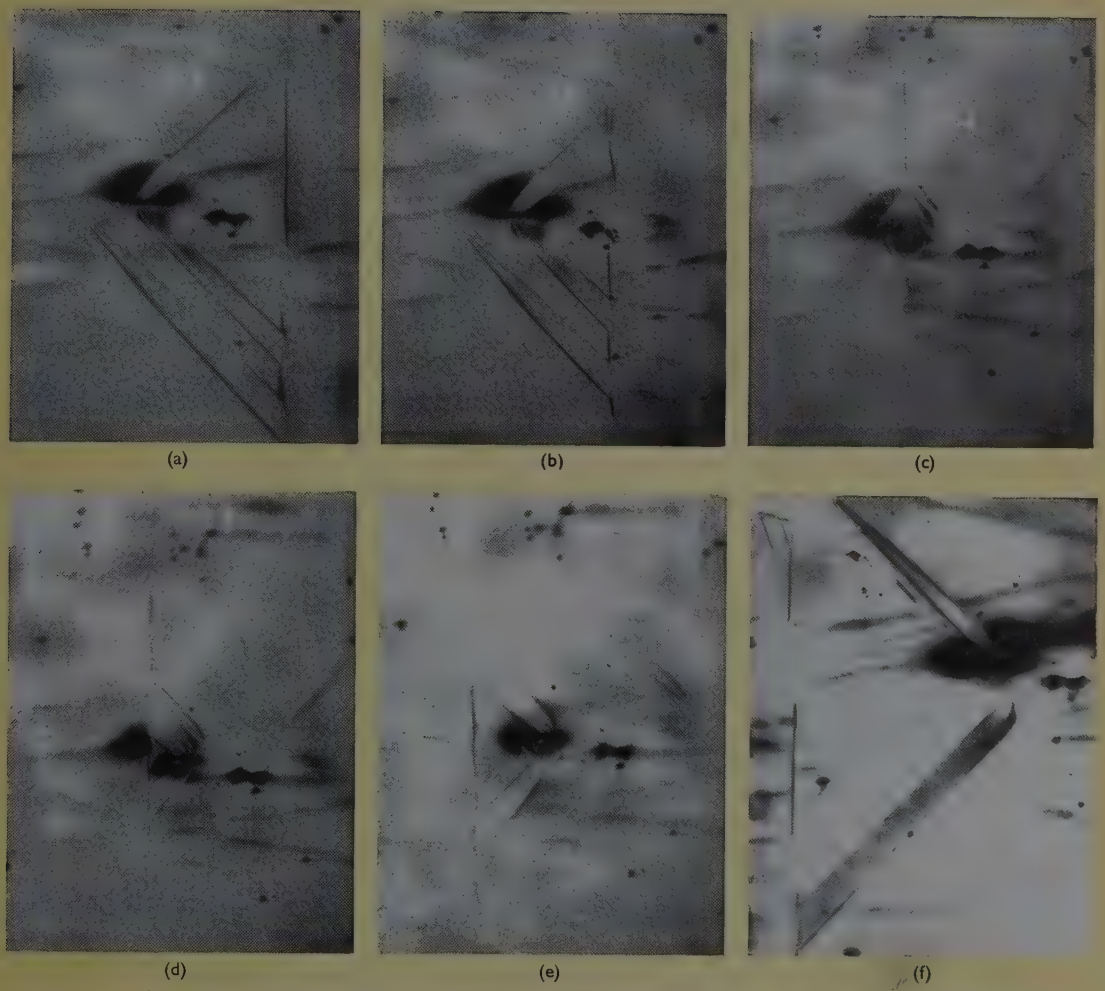

FIGURE 13 – *Patterns on silicon-iron illustrating passage of a* 180° *wall across a small pit in the crystal surface; sequence from* (a) *to* (f). *Wall moves from right to left.* (× 250). *(Note tree patterns around hole in* (c).)

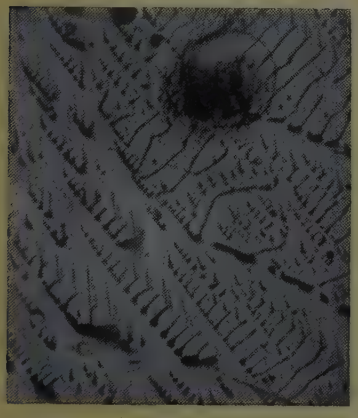

FIGURE 14(*a*) – '*Tadpole*' *patterns on polycrystalline silicon-iron grain with approximate* (110) *surface. A grain boundary is off the picture to the right.* (× 100)

FIGURE 14(*b*) – '*Tadpoles*' *and* '*lozenges*' *on an approximate* (110) *plane of silicon-iron with a small field applied along a* [110] *direction.* (× *c.* 100)

FIGURE 15 – *Echelon structure observed on a* (100) *surface of a rectangular block crystal of silicon-iron. Edge of block is at left edge of the photograph.* (× 90)

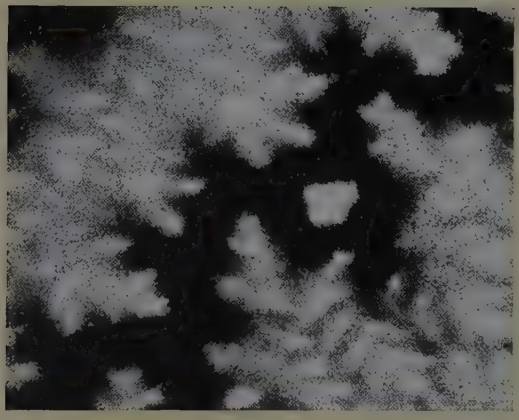

FIGURE 16 – *Detail of pattern on basal plane of cobalt.* (× 7800)

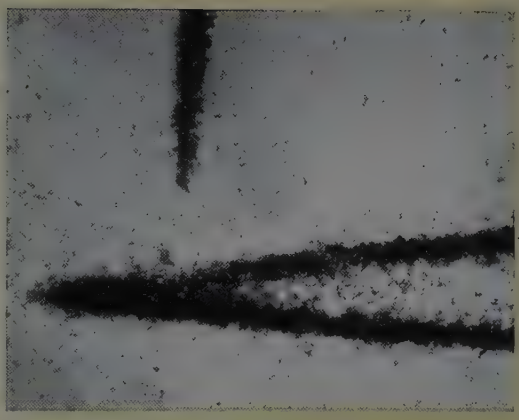

FIGURE 17 – *Tip of dagger closure domain on cobalt. Scratch in upper portion of picture.* (× 5900)

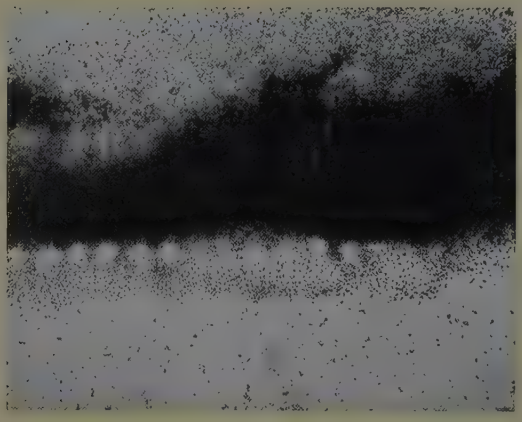

FIGURE 18 – *Scratch on cobalt surface.* (× 5000)

FIGURE 19 – *Strain pattern on cobalt crystal surface.* (× 5900)

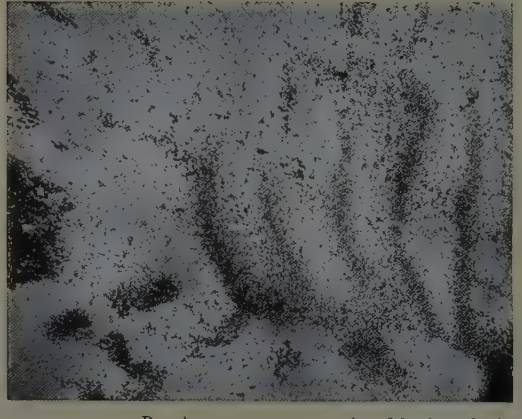

FIGURE 20 – *Powder pattern on a grain of barium ferrite (Magnadur).* (× 5000)

FIGURE 21 – *Pattern on the basal plane of a plate-shaped grain of barium ferrite.* (× 5900)

'spike' closure domain with the surface, and a satisfactory model of their formation can be given.

Further information about these structures was obtained by P. F. Davis [18] using large-grained specimens of silicon-iron whose surfaces were approximately (110) planes. W. S. Paxton and T. G. Nilan [19] had found lozenge-shaped patterns when a thin surface was inclined at an angle of between 4° and 7° to a true (110) plane, the specimen being either in a demagnetized or a weakly magnetized state. In figure 14(*a*) many tadpoles, and in figure 14(*b*) many lozenges, are to be seen. It is thought that lozenges are formed by the intersection with the surface of domains of reverse magnetization situated in the principal domains, which in thin specimens are arranged in layers, almost parallel to the surface, alternately magnetized in opposite directions (i.e. parallel to the [001] and [00$\bar{1}$] directions). The lozenges are therefore perpendicular to the [110] direction; individual tadpoles set parallel to the [111] direction. At an international conference held in Moscow [23] in 1956, Shur showed records of lozenge patterns obtained on sheets of silicon-iron some 6 to 50 μ in thickness; he emphasized that, even when the material is saturated, the lozenges do not completely disappear. This would mean that nuclei for domains of reverse magnetization are always available.

Martin found that when a rectangular block specimen of silicon-iron, with every face a (100) plane, is cut so that one end of the block terminates in a (111) surface, a very complicated 'echelon' pattern, with an extremely fine texture, was found on the (100) surface in the demagnetized state. A model indicating how such a pattern may be formed is shown in figure 22, and an excellent photograph of such a pattern is given in figure 15. Martin [20] has used the model in a calculation of the optimum domain size and its dependence on crystal size. He found that for a block specimen of rectangular cross-section with (111) planes at *both* ends it is nearly the same as that for a similar specimen with (010) faces at both ends, and that even if 180° boundaries are replaced by 90° boundaries the change in energy involved is very small. This remarkable result must influence our views of magnetization processes.

ELECTRON MICROSCOPE STUDIES

A new technique which appears to have great possibilities has recently been devised by D. J. Craik [21], who is able to prepare a kind of thin film replica of a domain pattern and to remove it from the metal surface for examination with either a light or electron microscope. For this purpose colloidal magnetite is prepared according to the Elmore recipe and peptized sufficiently for it to pass through fine filter paper. To the filtered solution 0·1 per cent of a commercial methyl ether of cellulose ('Celacol') is added, and any free acid is removed by repeated dialysis with distilled water. A drop of the treated solution dries to form an amorphous film a few hundred Ångströms thick.

Upon the metal surface to be examined is placed a thin film of Formvar resin some 200 Å thick; if necessary, the metal surface can be protected from rusting, etc., by first depositing on it a fine layer of quartz by evaporation *in vacuo*.

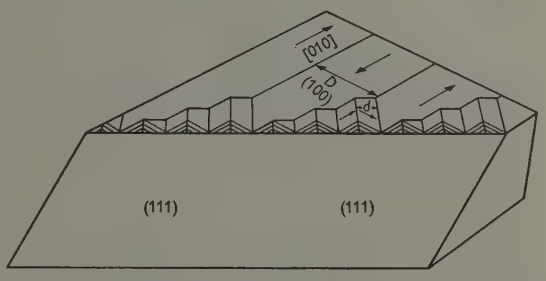

FIGURE 22 – *Model to illustrate 'echelon' pattern formation on* (100) *plane of silicon-iron.*

Sufficient colloid is placed upon the resin film to form a layer about 500 Å thick. The Bitter pattern is formed, and the colloid is allowed to dry *in situ*. The film is removed by placing a few drops of a thick solution of collodion in amyl acetate upon it; when this has dried, the whole may be detached freely. The record so obtained is permanent. Chosen portions of the record are now placed, with the collodion surface downwards, on the standard copper grids used in electron microscopy. These are placed on strips of stainless steel mesh, below which amyl acetate may be introduced to dissolve away the collodion.

Photographs illustrating the excellence of this new technique are shown in figures 16–20. Figure 16, which may be compared with figure 6, shows some of the fine detail in the powder pattern obtained on the basal plane of a cobalt crystal in the demagnetized state. Figure 17 is a record of the tip of a dagger-shaped closure domain, or domain of reverse magnetization, running horizontally, together with a scratch in the upper portion of the picture. A better example of a photograph of a scratch is seen in figure 18. The lower

border of the scratch is edged with fine hexagonal deposits characteristic of strained cobalt; another strain pattern is reproduced in figure 19.

It is important to apply this new technique to the examination of materials whose domain features are less well known than those of cobalt. A start has been made, and in figure 20 we have a typical domain pattern recorded on a large grain of barium ferrite (Magnadur). The particle is about 5 μ thick; a grain boundary lies to the right and the hexagonal axis of the crystal runs approximately vertical in the plane of the photograph. The domain walls are about 1 μ apart.

When particles are so small that domain boundaries cannot exist within them, it follows that their magnetization can be reversed only by a difficult rotation process, and this means a very high value of the coercivity. Figure 21 shows a record of the pattern on the basal plane of a plate-shaped grain of barium ferrite about 5 μ across, taken in the course of a study on domain patterns on grains which approach the critical size below which domain boundaries are impossible.

CONCLUSION

The foregoing account suffers from certain omissions due to lack of space. For example, no mention is made of patterns on nickel, whose study is difficult because the face-centred crystal possesses eight directions of easy magnetization, the [111] directions, and because its properties are so profoundly influenced by strain. Yet very beautiful pictures have been obtained by Japanese workers [22]. No mention is made of the maze patterns which are found on surfaces from which the Beilby layer has been only partially removed by electrolytic means, and whose study has recently provided additional information about closure domains [23]. Some beautiful and fundamental experiments on polycrystalline sheets of Perminvar [24] are not described, although these have shown how a single domain wall may be caused to form a closed path within a surface on a ring of the material. Experiments on permanent magnet materials [12] have also been omitted. But it is hoped that enough has been written to prove that the Bitter figure technique has enabled us to establish the correctness of the domain concept and to obtain much new information concerning important magnetic processes of which we were previously ignorant.

ACKNOWLEDGMENTS

The author would like to thank all those who have collaborated with him in these researches and in producing the pictures used in this article. The photograph of figure 14(*b*) was taken by Dr A. Hart, those of figures 16–21 by Mr D. J. Craik, and the remainder by Mr P. F. Davis and Mr P. M. Griffiths.

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Gibberellic acid

P. W. BRIAN and JOHN FREDERICK GROVE

Although it has been known for some thirty years that a metabolic product of the fungus *Gibberella fujikuroi* has a striking effect on plant growth, it is only comparatively recently that it has received detailed investigation. Research has now established the main chemical features of the biologically active substance and has elucidated its effects on the growth of plants. While the properties of gibberellic acid have naturally evoked much speculation about its practical applications in agriculture, no major applications have yet been found.

INTRODUCTION

In all countries where rice is grown, a soil-borne disease of rice caused by the fungus *Gibberella fujikuroi* (conidial state: *Fusarium moniliforme*) has been recorded. In most respects the symptoms of the disease are not unlike those of many other *Fusarium* diseases; the fungus enters through the roots and stem-base, causing local necrosis, and as it spreads in the host tissues the vascular system of the shoot turns brown and the shoot wilts. Many infected seedlings eventually die. But one early symptom is unique: the stems and leaves of some infected seedlings elongate more rapidly than those of healthy plants, so that an infected field looks as though it had been sown with a mixture of tall and short varieties of rice. This disease has been much studied in Japan and Formosa, where it is known as the bakanae disease.

Thirty years ago the Japanese plant pathologist E. Kurosawa [1] made the important discovery that cell-free filtrates made from pure cultures of *G. fujikuroi* grown on synthetic media would, if applied to healthy rice seedlings, produce the elongation symptoms characteristic of the disease. It therefore seemed almost certain that a metabolic product of the fungus, produced when it grew in either the host plant or in culture media, was responsible for the enhanced growth.

This observation was rapidly followed up in Japan, and it was soon shown that many other species of plant responded by extra growth. The effects observed were confined to shoot growth: root growth was either unaffected or slightly depressed. The conditions of production of the active material were studied, using the response of rice seedlings as a crude form of bioassay. Work on extraction and purification of the active material proceeded at the same time, and it was found that it could be adsorbed on charcoal and eluted with certain organic solvents. Eventually, in 1939, a crystalline material was obtained, in yields of about 10 mg per litre of crude culture media, which would stimulate growth if applied to the roots of seedlings in concentrations of a few parts per million; this was named gibberellin A [2]. Further work on the chemistry of gibberellin A and on its physiological properties was published in Japan, but because of the war it did not become known in Europe or America until several years after publication.

More recently, interest in the growth-promoting metabolites of *Gibberella fujikuroi* has spread, and from this increased attention has resulted the discovery of three related active compounds, each of similar physiological activity: these are now known as gibberellin A_1, gibberellin A_2, and gibberellic acid [3]. The last-named component, gibberellic acid, was first obtained in pure form independently, and almost simultaneously, in Britain and the United States. Gibberellic acid can now be produced in much greater yields than either gibberellin A_1 or A_2, and more detailed and fruitful work on its chemistry, physiological activity, and possible practical uses has been carried out than was possible with the original gibberellin A. The present article deals mainly with this more recent work.

PRODUCTION OF GIBBERELLINS AND GIBBERELLIC ACID

The earlier Japanese production method was based on surface culture of *Gibberella fujikuroi* on liquid media. Precise compositions of the media used were not published, but they appear to have been simple glucose/salts or glycerol/salts media, with ammonium chloride as the source of nitrogen. The cultures were incubated for 30–45 days at 25° C. The active material was isolated from filtrates of such cultures by a rather complex procedure. The basic step in the isolation was adsorption of the active material on carbon, from which it was eluted with methanolic ammonia. A

purification procedure consisting of several stages followed. Yields of about 10 mg per litre of 'crude gibberellin crystals' were obtained [4].

The development of stirred and aerated deep fermentation techniques for antibiotic production suggested that these methods might be used for gibberellic acid production. Japanese workers, using a single-stage fermentation and the same culture medium as they had used for surface culture, obtained yields not exceeding 8 mg per litre in a fermentation lasting 96 hours at 27° C. Using a three-stage fermentation with a 1·5–2·0 per cent glucose/salts medium, an American group obtained yields of 17 mg per litre of mixed gibberellin A and gibberellin X (= gibberellic acid) in a fermentation at 25° C whose total duration was 95 hours. Their media and extraction methods were essentially similar to those used by Japanese workers [3, 5].

Much greater yields of gibberellic acid, approaching 200 mg per litre, have been described by a British group [6] using a single-stage stirred fermentation. Though they used a different strain of the fungus, it is most probable that changed fermentation conditions were mainly responsible for the increased yield. These changes involved (*a*) use of a medium with higher sugar content (4 per cent glucose or sucrose), and (*b*) use of much longer fermentation times, maximum yields being obtained in 18 days at 25° C. These workers found that although glycerol media supported good growth, they were inferior to sucrose or glucose as sources of carbon for the production of gibberellic acid. Their method of extraction was somewhat simpler than the Japanese method, though it was basically similar; the gibberellic acid was removed from culture filtrates by adsorption on carbon, from which it was eluted with aqueous acetone.

EFFECTS OF GIBBERELLIC ACID ON EXTENSION GROWTH OF PLANTS

Shoot growth. The mode of application of gibberellic acid is not critical. Essentially similar responses are elicited if it is sprayed on the shoot as a whole, if applied to any single leaf in a microdrop of water or alcohol, or if the roots are treated by including gibberellic acid in the soil or culture solution. The microdrop application to leaves is convenient in quantitative work.

The types of growth response are best described by reference to a few examples. Wheat seedlings are increased in height (figure 2). This is due to increase in length of both stem internodes and leaves. The leaves may be as much as 50 per cent longer than those of untreated plants, but are somewhat narrower and usually paler in colour. This chlorosis is most marked in plants growing in soils or culture solutions of low nutrient value. If no mineral nutrients are limited, the reduced depth of colour is transient. Such quantitative data as have been published [7] refer to the application of gibberellic acid to roots; in such experiments an effect can be detected when gibberellic acid is present in the nutrient to the extent of 0·1 μg per ml, and maximal effects are produced by 1–10 μg per ml. In experiments in which wheat plants were sprayed weekly with gibberellic acid (100 μg per ml) until maturity, the mean height of the flowering stems was increased by 25 per cent. There were, however, rather fewer ears, this being associated with a 25 per cent reduction in the total number of tillers produced. The ears emerged from the sheathing leaves a few days before those on untreated plants.

The growth of dwarf varieties of garden pea (*Pisum sativum*) is greatly stimulated by gibberellic acid. Stem internode length may be increased by 200–400 per cent; leaf petioles are increased in length to much the same extent, but leaf size is not so much affected as in wheat and other cereals. Though treated plants are at first somewhat paler in colour than normal, this effect is less noticeable than in cereals. Quantitative data relating dose and response are available for the dwarf pea [8]. An obvious effect is produced by a dose of 0·01 μg per plant; above this level the response is linearly related to the logarithm of the dose in the range 0·01–0·1 μg (figure 1). The response to a single dose is temporary. Immediately after application, growth is accelerated: the size of the dose applied does not greatly influence the newly established growth rate, but does influence the time over which this accelerated growth is maintained. Eventually, growth rate slowly subsides to that of untreated plants (figure 3). To maintain an increased growth rate over the whole life cycle of a plant, gibberellic acid must be applied at fairly short intervals. In an experiment in which dwarf pea plants received weekly doses of 1 μg gibberellic acid, the final height was increased by 50 per cent, but the total number of stem internodes was unchanged [9]. Thus the effect of gibberellic acid on the pea plant is to increase height solely by increasing internode length. Moreover, this increase in internode length is almost entirely due to increased cell extension; there is little evidence of increased cell multiplication.

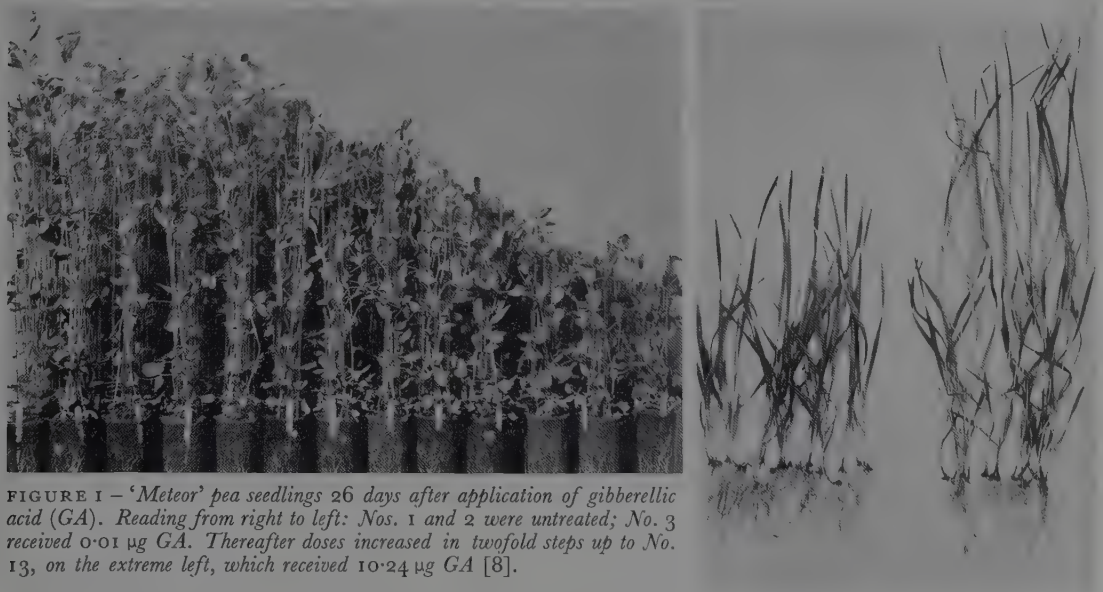


FIGURE 1 – *'Meteor' pea seedlings 26 days after application of gibberellic acid (GA). Reading from right to left: Nos. 1 and 2 were untreated; No. 3 received 0·01 μg GA. Thereafter doses increased in twofold steps up to No. 13, on the extreme left, which received 10·24 μg GA* [8].

FIGURE 2 – *(Right) Wheat seedlings grown in Pfeffer's culture solution (left), and (right) in a similar solution containing 2 μg per ml gibberellic acid.*

The effects of gibberellic acid on the 'Cupid' sweet pea (*Lathyrus odoratus*) (figure 4) differ in several respects from those just described for the garden pea. The 'Cupid' sweet pea is a very dwarf type, with a bushy habit and leaves much smaller and darker in colour than those of the more usual climbing sweet pea. Early in growth, when the main axis is about six inches high, further development of the main axis normally ceases, and some lateral buds develop into branches which may become as long as the main axis, thus giving rise to the bushy habit. Application of a weekly dose of 1 μg gibberellic acid completely alters the plant habit. In an experiment in which seedlings 3 cm high were treated in this way, growth of the main axis was much accelerated: after three weeks, untreated plants were 7 cm high and treated plants 42 cm high. At this point lateral branches developed rapidly on the untreated plants, but much less rapidly on the treated plants. The general growth picture after 7 weeks' growth is shown in table 1. Whereas untreated plants had developed six side branches, each roughly of equal length and having the same number of internodes as the main axis, growth in the treated plants proceeded predominantly in the main axis, which was about ten times taller than that of the untreated plants. The total number of internodes formed was not altered. The leaflets were altered in colour and shape, becoming pale green and lanceolate, as is usual in climbing sweet peas, instead of dark green and ovate. Moreover, the surface area of each leaflet was approximately doubled. An effect of this kind on leaf area is unusual in dicotyledons. This change in growth habit, from dwarf bushy plants to tall climbing ones, has also been noticed in dwarf beans [7, 10].

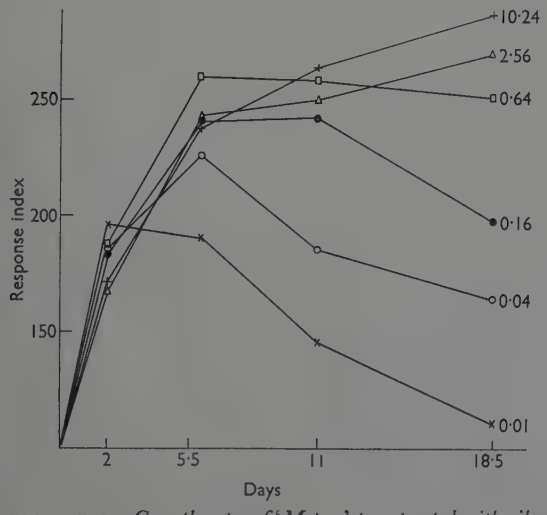
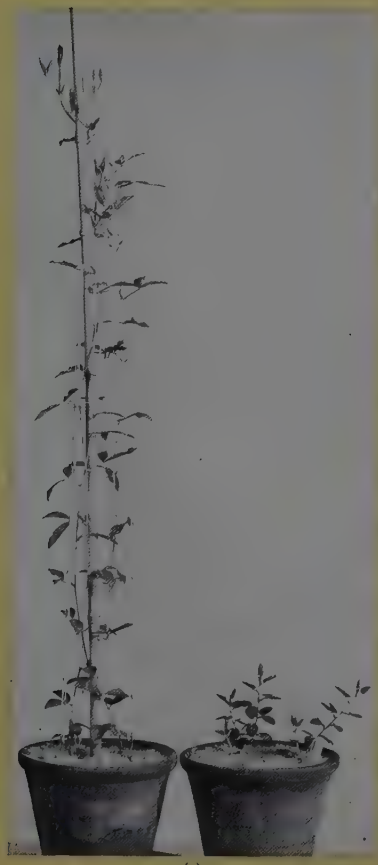


FIGURE 3 – *Growth rates of 'Meteor' peas treated with gibberellic acid, expressed as percentage of that of untreated plants. Doses of gibberellic acid (μg) are indicated on the right* [8].

Such increases in shoot height are often accompanied by increases in the fresh and the dry weight

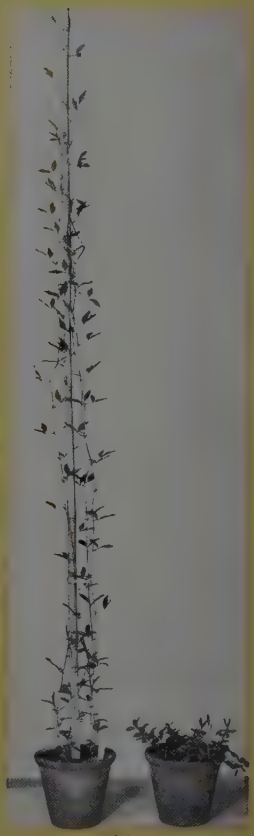
(a)

(b)



(c)

(d)



(e)

FIGURE 4 – *Effect of doses of* 1 μg *gibberellic acid weekly on growth of 'Cupid' sweet peas.* (a) 2 *weeks;* (b) 3 *weeks;* (c) *and* (d) 4 *weeks;* (e) 7 *weeks after first treatment. The effect on the shape of leaves is shown most clearly in* (d). *Plants treated with gibberellic acid are on the right in* (a) *and* (b), *and on the left in* (c), (d), *and* (e).

TABLE I

Mean effect of weekly doses of 1 μg *gibberellic acid on growth of 'Cupid' sweet peas.* (Measurements made after 7 weeks' growth)

Treatment	Height (cm)	Number of internodes in main axis and all branches	Number of internodes in main axis	Number of branches
None ..	12	83	14	6
1 μg weekly	122	82	43	4

of shoots. For example, increases of 24 per cent in dry weight of wheat seedlings and of 15 per cent in pea seedlings have been recorded in small-scale experiments with plants growing in culture solutions containing gibberellic acid. Increases of over 40 per cent in dry weight of grass yields in field plots have resulted from a single sprayed application of gibberellic acid. The cause of this increased yield has not been critically studied, but it seems probable that it is a secondary result of increased area of leaf and other photosynthetic surfaces. Increases in weight are marked only where initial nutrients are not so low as to limit growth. Even where the weight of plants as a whole is not increased, there may be a redistribution as between root and shoot so that shoot weight is increased and root weight decreased. This is particularly noticeable where there is nutrient deficiency [7, 10, 11].

A large number of species have recently been treated with gibberellic acid in simple observational experiments, and in most cases responses of the kind described above have been elicited; however, some plants do not respond at all, and in others such responses as have been seen are small [10, 12]. This variation in response is discussed further in a later section of this article.

Root growth. Root growth is not stimulated by gibberellic acid under any known circumstances. This is surprising and suggests that, contrary to what has usually been supposed, growth regulation in shoots and roots is in some respects essentially different. In relatively high concentrations gibberellic acid slightly inhibits root growth [8].

COMPARISON WITH AUXINS

The increased shoot growth induced by gibberellic acid is mainly attributable to cell extension. Cell extension in plants is already known to be controlled by hormones called auxins [13], the best known of these being 3-indolylacetic acid. Many bioassays of auxins, notably the coleoptile-section straight-growth tests, are in fact based on the capacity of auxins to induce cell elongation. A detailed comparison of the physiological properties of gibberellic acid and indolylacetic acid reveals some interesting differences [9, 14, 15].

An important difference is to be seen in the effect of the two substances on extension of etiolated coleoptile sections. Indolylacetic acid very greatly increases the extension of such sections in the usual 24-hour observation period; the relation between amount of extension and the logarithm of the dose is approximately linear within the range 0·01–1·00 μg/ml. Gibberellic acid, however, induces very little extension, and the dose-response curve flattens off very rapidly. Similarly, indolylacetic acid induces marked extension of internode sections in peas grown in the light, but gibberellic acid does not. We thus have the striking paradox that while gibberellic acid induces big extensions of growing tissues in intact wheat or pea plants, on which indolylacetic acid has little effect, with sections excised from growing zones of these plants the reverse is the case.

The auxins, in addition to their effect on cell extension, also affect cell division, stimulating cell proliferation in some tissues. For instance, treatment of cuttings with auxins accelerates root initiation. Gibberellic acid does not do this; indeed, it antagonizes the root-initiating effects of auxins.

If the main growing point of a plant is excised, one or more lateral buds commence to grow to take its place. If an auxin is applied to the decapitated top of the main shoot, development of the laterals is inhibited. Gibberellic acid has no such effect; indeed, it stimulates more rapid development of the laterals. But in those intact plants in which the main axis ceases to extend and laterals consequently develop, as in the case of the 'Cupid' sweet pea mentioned earlier, gibberellic acid applications enable the main axis to continue growth and formation of laterals is inhibited.

There are several other noteworthy differences. For instance, auxins inhibit leaf abscission; gibberellic acid does not. Excessive doses of auxin induce abnormal cell proliferation in some tissues; gibberellic acid does not.

All these striking differences between gibberellic acid and auxins lead naturally to the view that the two classes of substance must act differently.

Nevertheless, both induce cell extension under appropriate conditions, and it remains possible that in producing this effect they may act similarly. It has been shown [16] that extension of sections from growing internodes of peas is stimulated by auxins but not by gibberellic acid, but that in the presence of indolylacetic acid, gibberellic acid produces an extra amount of extension over and above that produced by optimal concentrations of the auxin. Thus gibberellic acid depends for its activity on the presence of indolylacetic acid. This probably explains why it produces a response in whole plants, with their auxin synthesizing system intact, but produces at most a slight response in auxin-depleted sections. The balance of evidence at present lies in favour of the view that the effect of gibberellic acid on growth is in some way distinct from that of the auxins, but that the two are complementary.

FURTHER PHYSIOLOGICAL EFFECTS OF GIBBERELLIC ACID

We have so far described the effects of gibberellic acid on vegetative growth of plants whose requirements for normal growth and development are not critical. But many plants develop normally only if exposed, at suitable times during their life cycle, to certain quite specific stimuli. Not only vegetative growth may be so conditioned, but flowering may be even more affected. A preliminary study has been made of the effects of gibberellic acid on some plants of this kind, and the results are of particular interest.

There is a large class of plants which may be described as cold-requiring biennials. It includes several familiar crop plants, such as some members of the cabbage family, carrots, parsnips, and sugar-beet. In the first season of growth, in their natural habitats, such plants form a basal rosette of leaves, with negligible development of a stem axis. In the second year of growth, an elongated stem develops on which flowers are borne. Neither stem nor flowers are produced unless the plant is first exposed for a short period to a low temperature, the critical temperature varying from species to species. This stimulus is normally a consequence of winter conditions, but if applied artificially production of the stem axis will commence immediately, even in the first season of growth. Further growth of this axis, and production of flowers, is often also conditioned by the length of day. A. Lang [17] has described some effects of gibberellic acid on the growth and development of the common henbane (*Hyoscyamus niger*), a cold-requiring biennial which also needs long days for complete development to the flowering stage. He found that fairly large doses, between 60 and 300 μg per plant, would induce formation of a stem in plants at the rosette stage if they were kept at temperatures well above that which normally induces such development, but that under the same conditions untreated plants all remained in the rosette stage. However, the effect of gibberellic acid was more marked in plants exposed to long daily lighting than in those exposed to short days; a dose of 60 μg had little effect on plants kept in short days, but markedly promoted stem extension of plants in long days. Larger doses promoted stem elongation even of plants grown in short days. Thus relatively small doses of gibberellic acid appear to replace the low-temperature stimulus completely, but much larger doses are required to replace the long-day requirements for normal stem extension. Differential effects on the growth of plants in long and short days have also been described for two annual plants [18]. The North American weed *Galinsoga parviflora* responds to gibberellic acid more in long days, but the corn-cockle (*Agrostemma Githago*) responds more in short days.

The *Hyoscyamus* plants treated with gibberellic acid in long days flowered normally; those grown in short days failed to flower, in spite of the production of a stem. Thus, of the conditions normally necessary for induction of flowering, gibberellic acid replaces the cold treatment but not the long days. This result is highly significant for two reasons. Firstly, it has been possible to achieve a clear distinction between the mechanisms of control of stem elongation and flowering. Secondly, this is the first case, with one exception, of chemical induction of flowering under strictly non-flowering environmental conditions. The one exception is the pineapple, which may be induced to flower by auxin treatment [13], but the flowering behaviour of the pineapple is in many respects anomalous.

Gibberellic acid also breaks dormancy of some seeds and tubers. For example, it induces sprouting of dormant potato tubers, and induces germination of dormant lettuce seeds which normally germinate only if exposed to red light [14, 19]. Auxins do not break dormancy, but gibberellic acid certainly is not unique in doing so; similar effects are sometimes produced by unsaturated hydrocarbons, ethylene chlorhydrin, and certain sulphur compounds such as thiourea or glutathione. It seems most improbable that the mechanism of action is the same for all these types of compound.

Gibberellic acid thus appears to influence many physiological processes besides extension growth, but too little experimental work has yet been done for us to be sure whether some of these effects are general or are merely anomalous individual effects.

IS GIBBERELLIC ACID A NATURAL PLANT HORMONE?

Stem extension, flowering, and breaking of dormancy of seeds and tubers are not obviously physiologically related processes, yet, in some plant species at least, gibberellic acid stimulates all these. It seems remarkable that a fungal metabolic product—produced, as far as is known at present, by a single species of fungus—should intervene in so many aspects of plant growth and development. It is remarkable, too, that none of its effects are abnormal, since most of them can also be induced by appropriate light and temperature conditions in the plant's environment. The physiological properties of gibberellic acid could be much more readily understood if it were structurally or physiologically related to some natural plant hormone or hormones: there is evidence that this may indeed be so.

First, there is genetical evidence. We have already mentioned the effect of gibberellic acid on the 'Cupid' sweet pea. This plant, which originally arose from a sweet pea of the normal climbing type by recessive mutation of a single gene, has smaller leaves, shorter internodes, and a more branched habit than the climbing type. Gibberellic acid treatment alters the growth form so that it approximates to that of the climbing sweet pea; it has no effect on climbing sweet peas themselves. Dwarf varieties of garden pea when treated with gibberellic acid assume the habit of tall peas [8], but tall peas are little affected by gibberellic acid. Here again, the dwarf plant is recessive to the tall, differing from it in a single gene. Some single-gene recessive dwarf mutants of maize assume the normal tall habit after treatment with gibberellic acid [20], but tall varieties are not affected. In each of these cases, and others could be cited, a recessive dwarf variety is induced by gibberellic acid to assume the growth habit of the tall variety from which it originally arose by mutation. Such instances are well known in microbial genetics. Thus, spores of the mould *Neurospora*—which will grow on a simple glucose/salts medium—if treated with X-rays will give rise to some mutant colonies which will no longer grow normally on the glucose/salts medium but need also aneurin (vitamin B_1). Such strains, called 'aneurinless', are recessive to the wild type and differ from it in a single gene. Biochemically, they differ from the wild type in that, unlike the latter, they are not able to synthesize aneurin in sufficient quantity to maintain normal growth. By analogy, it is reasonable to explain the differential response to gibberellic acid of dwarf and tall varieties of plant by assuming that the dwarfs have lost the power to synthesize some substance, hormonal in nature, that can be replaced by gibberellic acid. It may be mentioned in passing that this is perhaps the first record of the effects of a mutation in a higher plant being reversed by supplying a specific chemical substance.

Secondly, there is more direct biochemical evidence. In 1951, before interest in the gibberellins had spread beyond Japan, J. W. Mitchell, D. P. Skaggs, and W. P. Anderson [21] showed that ether extracts of immature dwarf bean seeds contained substances which would stimulate elongation of the epicotyls of dwarf bean seedlings to a degree much exceeding that following auxin application. Following up this observation, it has been found that such seed extracts induce growth of dwarf mutant maize and dwarf peas precisely as gibberellic acid does. The active material moves in chromatograms in the same way as gibberellic acid [22]. Similar materials have been found in shoots of tall and dwarf pea seedlings [23]. It is not yet known whether there is more of this substance in tall than in dwarf pea shoots, but if this were found to be so, the interpretation of dwarfness as a failure to synthesize sufficient of a hormone resembling gibberellic acid would be greatly strengthened.

Let us assume for the moment that the existence of such a hormone in plants is established. We can then envisage growth and other aspects of development as being regulated by a balance of auxins and the hormone. We already know that growth, flowering, and dormancy phenomena are in some way bound up with auxin metabolism, but it has never been possible to explain them solely in such terms, just as dwarfness is inexplicable in terms of auxin alone [24]. It already seems possible that much more will be explicable in terms of an interacting system of the two kinds of growth hormone, possibly acting in association also with inhibitor systems. The work that will prove the worth of such speculations as this is still in progress, but it is interesting to reflect that these new possibilities have arisen largely as a result of the simple observations on bakanae disease of rice made by Kurosawa in 1926.

PROSPECTS OF APPLICATION

Naturally enough, the remarkable effects of gibberellic acid on plant growth and development have led to much speculation concerning its possible application in agriculture. This is a matter which can be settled only by field experiments; there is no *a priori* reason why it should be of practical use. Although indolylacetic acid has been found to play a most important role in controlling cell growth and cell multiplication in plants, it has found no use in agriculture, although structurally analogous substances, such as 2:4-dichlorophenoxyacetic acid, have found use as inhibitors of plant growth.

Possible applications of gibberellic acid can best be discussed in relation to the four types of physiological response described earlier in this article: (1) increase in dry weight of shoots, (2) increase in height of main-stem axis, (3) induction of flowering in biennials without need for a cold treatment (vernalization), and (4) breaking of dormancy.

Of these, the first is potentially of greatest importance. As we have seen, increases in fresh and dry weights of shoot tissues are sometimes obtained in small-scale laboratory experiments. The only detailed field work so far published is that of D. G. Morgan and G. C. Mees [11]. In their experiments, gibberellic acid in aqueous solution was sprayed on growing crops at a dose of 2 oz per acre. With most crops the results were disappointing, in so far as increased growth of stems and leaves was not accompanied by increased crop yield. This was true of tomatoes, blackcurrants, peas, and beans. Wheat crops treated in spring responded by more rapid growth soon after treatment but yields of grain and straw at harvest were unaffected. Yields of root crops were reduced. Only with grass were consistent yield increases obtained.

In experiments on grass swards at several centres, the grass was cut four to ten weeks after application of gibberellic acid at 2 oz per acre. Growth of all the plants in the sward was obviously accelerated, even under conditions in which fertilizers produced no response. This was accompanied by quite considerable increases in dry matter (table II). The nitrogen content of the grass was slightly lower than that of untreated grass, so that crude protein yields were not increased to the same extent as total dry matter. At first sight these results seem very promising. However, if the grass was allowed to grow for a further period the yields from treated plots were lower than those from untreated plots (table II), so that the net effect of treatment was negligible. The reason for this depressed growth at the second cutting was not obvious. These trials show the need for caution in extrapolating the results of laboratory experiments to field conditions.

TABLE II

Differences in the dry weight yields of grassland at two cuttings, following treatment with gibberellic acid [11]

Date of treatment	Dry weight yields at cutting 1			Dry weight yields at cutting 2		
	Untreated control (cwt/acre)	Increase (cwt/acre) due to 2 oz/acre GA	Increase as percentage of control	Untreated control (cwt/acre)	Decrease (cwt/acre) due to initial GA treatment	Decrease as percentage of control
1st March 1955 ..	19·8	3·1	16	30·8	3·9	13
4th March 1955 ..	12·2	4·0	33	13·5	3·0	22
14th March 1955 ..	29·8	4·3	14	29·2	3·7	13
18th March 1955 ..	9·1	3·9	43	13·2	2·4	18
18th March 1955 ..	11·3	1·6*	14	16·7	2·0	12
13th April 1955 ..	25·1	5·0	20	30·3	7·0	23
13th April 1954 ..	17·1	7·9	46	—	—	—
13th April 1954 ..	19·3	6·4	33	40·0	9·9	25
10th July 1953 ..	15·4	4·1*	27	4·4	0·5*	11
5th August 1954 ..	21·8	1·2	6	—	—	—
18th August 1954 ..	22·9	3·2	14	—	—	—

All differences, except those marked with an asterisk, were significant at the 1 per cent probability level.

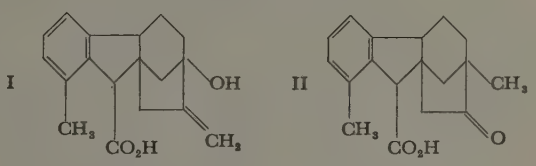
By lowering mechanical strength, increase in stem length will probably be more often deleterious than useful under practical conditions. For instance, the chances of being beaten down will be seriously increased in a cereal crop with abnormally long stalks. Where the crop is a biennial such as cabbage or lettuce, harvested in the rosette stage, stimulation of stem production, i.e. of 'bolting', would be obviously undesirable. There is, however, one instance where it might be a useful effect; that is in those crops, such as flax and hemp, where fibres are extracted from the stem. F. Lona and A. Bocchi [24] have shown in laboratory experiments that both internode length and stem length of hemp is increased by gibberellic acid, but it is not known whether such effects could conveniently be produced under field conditions, nor how the quantity and quality of the fibre would be affected.

Earlier flowering of biennial plants might be useful in production of the seed of certain crops, but it is not yet known whether Lang's laboratory experiments with *Hyoscyamus* can be repeated on a field scale with other biennials. Similarly, no practical experience in connection with dormancy breaking has been reported. We may therefore conclude that such field experiments as have been carried out do not yet indicate any major use for gibberellic acid in agricultural practice and that far more field experimental work will be needed before a sound assessment of the prospects can be made.

CHEMISTRY OF GIBBERELLIC ACID

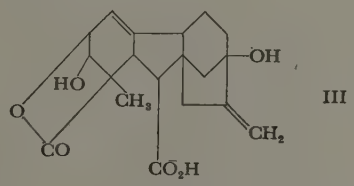
Gibberellic acid is a colourless monobasic carboxylic acid, melting with decomposition at 233–235° C; it is optically active ($[\alpha]_D^{20} + 92°$). Analysis and molecular weight determination show its formula to be $C_{19}H_{22}O_6$ [25]. It is evidently a dihydroxy acid, for it forms monoacetyl and diacetyl derivatives each of which yields a monomethyl ester, as does the acid itself. If the acid is allowed to stand with excess of alkali at room temperature a second equivalent of alkali is consumed: this, considered together with the fact that the infra-red spectra of the acid and its derivatives in dioxan solution show strong bands at 1780 cm^{-1}, indicates the presence of a saturated γ-lactone ring. Microhydrogenation shows the presence of two ethylenic bonds. The above evidence accounts for all the oxygen atoms and indicates that gibberellic acid is a tetracyclic dihydroxylactonic acid.

Further information about the ring system has in the main been gained from study of two products of acid hydrolysis. Mild acid hydrolysis (normal hydrochloric acid at 20° C) of gibberellic acid yields, among other products, *allo*gibberic acid ($C_{18}H_{20}O_3$), together with one molecule of carbon dioxide: if the hydrolysis is conducted at 100° C the *allo*gibberic acid is isomerized to gibberic acid. The available evidence, summarized below, allows the structure of these two hydrolysis products to be expressed with a good deal of confidence as:



allo*gibberic acid* *gibberic acid*

Determination of the structure of these two derivatives, however, does not make it possible to assign a definite structure to gibberellic acid itself. The evidence is consistent with the structure III, but other possibilities which have been summarized elsewhere [26] cannot at present be excluded. The stereochemistry of gibberellic acid and its structural relationship to gibberellins A_1 and A_2 remain to be elucidated.

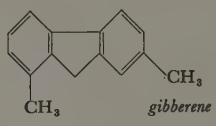


gibberellic acid

Gibberic acid. The formation of an oxime, a methyl ester, and an oxime ester shows this to be a keto acid; the infra-red spectrum, with a strong band at 1741 cm^{-1}, indicates that the keto group is present in a five-membered ring. It contains no ethylenic bonds, but the ultraviolet spectrum is consistent with the presence of a benzenoid ring.

Oxidation with selenium dioxide yields gibberdionic acid, $C_{18}H_{18}O_4$, a yellow cyclic α-diketone. The ultraviolet absorption spectrum of this is almost identical with that of gibberic acid in both ethanolic and sodium hydroxide solution. This is

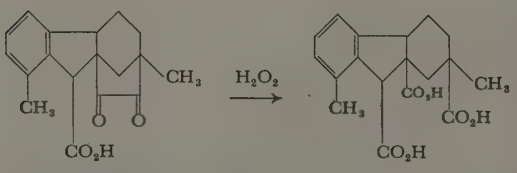
significant, for α-diketones in which adjacent carbon atoms carry hydrogen readily enolize and in consequence have an ultraviolet spectrum characteristically different from that of the parent monoketone. Gibberic acid therefore contains a $—CH_2—CO—$ grouping so situated in a five-membered ring that enolization is precluded.



gibberene IV

Oxidation to benzene-1:2:3-tricarboxylic acid and selenium dehydrogenation to a hydrocarbon, gibberene, which has been shown to be 1:7-dimethylfluorene (IV), establishes the presence of the 5:6:7:8:12:13-hexahydro-1:7-dimethylfluorene nucleus. Gibberene itself has been unambiguously synthesized [27] from 2-amino-5-methylbenzoic acid and *o*-tolyl magnesium bromide. The suggestion [28] that an acid obtained from gibberene might be fluorenone-4:5-dicarboxylic acid must now be discarded [29].

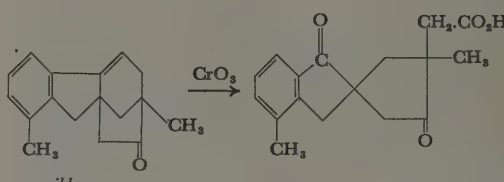
Evidently no skeletal rearrangement occurs during the selenium dehydrogenation, because gibberene is also obtained by mild dehydrogenation of the tricarboxylic acid (VI) formed by oxidation of gibberdionic acid (V) with alkaline hydrogen peroxide. The selenium dehydrogenation of gibberic acid must therefore involve elimination of the $—CH_2—CO—$ bridge, and so the methylene group of this bridge is attached to a quaternary carbon atom.



gibberdionic acid

V VI

The position of the methylene carbonyl bridge in gibberic acid is finally determined by the following series of reactions. Oxidation by permanganate yields dehydrogibberic acid, the ultraviolet spectrum of which indicates the presence of an ethylenic bond conjugated with the benzene ring. This acid can be decarboxylated to form a ketone, gibberone, with a five-membered ring. The latter retains the conjugated double bond, the position of which must be as in (VII), since oxidation with chromic oxide yields an alkali-stable indanone carboxylic acid. The constitution of this (VIII) can be deduced from the fact that on permanganate oxidation 3-methylphthalic acid and β-methyltricarballylic acid can be isolated.

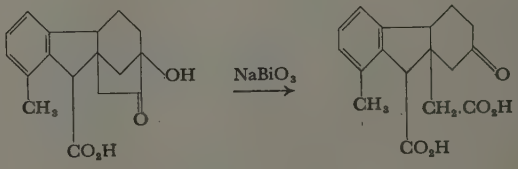


gibberone

VII VIII

Finally, the position of the carboxyl group in gibberic acid is established by dehydrogenation of methyl gibberdionate to methyl 1:7-dimethylfluorene-9-carboxylate identical with a synthetic specimen.

Allo*gibberic acid*. This contains a benzenoid ring, a terminal methylene group, and one hydroxyl group which appears to be tertiary both because it is difficult to acylate and because dihydro*allo*-gibberic acid cannot be oxidized to a ketone. A Wagner-Meerwein rearrangement would explain the isomerization to gibberic acid. The position of the carboxyl group is as in gibberic acid, since methyl *allo*gibberate yields methyl gibberate with dilute acid. Ozonolysis of *allo*gibberic acid yields formaldehyde and a five-ring α-ketol (IX) which sodium bismuthate will oxidize to a dicarboxylic acid (X). The dicarboxylic acid, on selenium dehydrogenation, yields 7-hydroxy-1-methyl-fluorene identical with a specimen obtained synthetically from 2-amino-5-methoxybenzoic acid by a route similar to that used for the synthesis of gibberene [30].



IX X

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Book reviews

ORGANIZATION OF SCIENCE

The Organisation of Science in England, *by D. S. L. Cardwell. Pp. ix + 204. William Heinemann Limited, London.* 1957. 18*s. net.*

Mr Cardwell has performed a very useful service. He has recorded the development of scientific and technical education in England from 1800 to the end of the first world war. His chronicle is well documented; he has given accurate summaries of the chief features of this confused and fascinating story; and he has picked out the names of some of the men who should be honoured as the pioneers of education in science—Brougham and Birkbeck, Babbage and Lyon Playfair, James Hole and Booth. There is a good account of the part played by the mechanics' institutes, the Royal Society of Arts, the British Association, and the select committees and royal commissions which followed the Great Exhibition of 1851.

Mr Cardwell has wisely refrained from too many explanations or rationalizations of the facts in his chronicle. Almost every page raises questions. Why did technical education in England develop so differently from that in Germany? Why, if technical education was so much more advanced on the Continent in the 1860s, did one find English craftsmen commonly employed in continental firms? Did the reluctance of Oxford and Cambridge to reform themselves in mid-century retard or accelerate the rise of provincial universities in England? And so on. It will need a much more thorough study (especially of foreign sources) than Mr Cardwell has succeeded in making, to answer such questions as these; but he has drawn attention to them, and that is a welcome and significant contribution.

The book so closely covers ground already treated by Professor Armytage in chapters 8–11 of his 'Civic Universities' that comparison is inevitable. Mr Cardwell does not write with the same precision and clarity as Professor Armytage, nor does he display such an easy mastery over his facts. There are some minor and irritating sub-editorial inconsistencies, e.g. some names appear adorned with initials, titles, and even degrees; other names, entitled to all these embellishments, are not so favoured. A much more serious defect is that the index, which is an essential part of such a chronicle as Mr Cardwell's, is very poor. However, these are quibbles: the book is a very useful contribution to the history of education and the author is to be congratulated on reducing so much material to order in such a modest compass. E. ASHBY

RELAXATION METHODS

Relaxation Methods in Theoretical Physics, *Vol. II, by Sir Richard Southwell. Pp. vi + 522. Clarendon Press, Oxford.* 1956. 55*s. net.*

This is the second volume of a treatise of which Volume I was published in 1946. That volume dealt with plane potential problems, problems of conformal transformation, and problems involving boundaries or interfaces whose positions are not finally known. The present volume deals with a number of more difficult problems which could not be included in the earlier volume, since they had not been released from the restrictions of wartime secrecy. They relate to biharmonic analysis, to stress systems in solids of revolution, to eigenvalues, and to certain aspects of elastic stability; a number of interesting non-linear problems of elasticity, hydrodynamics, and plasticity are also dealt with. The present volume is of very great interest not only for the variety of important problems of mathematics and engineering which it considers, but for the technical advances in relaxation methods which it describes. The volume is beautifully printed and illustrated.

A certain air of sadness broods over this volume, in which the author seems at last to bid farewell to his readers. No one is better entitled to assert that his purpose is at last achieved, but it is greatly to be hoped that Sir Richard Southwell will find new worlds to conquer and further works to publish.

G. TEMPLE

SOLAR PHYSICS

The Sun, *by G. Abetti, translated by J. B. Sidgwick. Pp.* 336. *Faber and Faber, London.* 1957. 63*s. net.*

Since Professor Abetti's book *Il Sole* was first published in 1934 it has provided the most complete account available of the complicated facts about the spots and other features of the solar surface, and about their changes of form and position. It has become a standard work of reference, of which an English translation was published in 1938.

A second Italian edition, revised and enlarged, appeared in 1951. During the interval between the two editions there were great advances in solar physics. In particular, the importance and significance of solar flares have been recognized and they have been intensively studied; solar radio emissions from the quiet sun and the enhanced emissions from disturbed areas have been discovered and investigated; the origin of the coronal spectral lines has been found and much study has been devoted to the physics of the corona; much has been learnt about the constitution of the Sun and about the source of stellar energy.

The publication in English of a translation of the second edition is very welcome. Progress in solar research has been so rapid that some revision of the work, and additions to it, were needed: this has been carried out by Professor Abetti for the purpose of the new translation. The new edition provides an up-to-date survey of what is known about the Sun. It can be read with profit by both the amateur and the professional student. The value of the book is much enhanced by the numerous plates, which have been carefully selected to illustrate observational equipments and various solar phenomena. There are, in addition, 97 text figures. H. SPENCER JONES

MODERN PHYSICS

An Approach to Modern Physics, *by E. N. da C. Andrade. Pp. ix* + 232. *G. Bell & Sons Ltd., London.* 1956. 25*s. net.*

This volume is an extensively revised and enlarged version of Professor Andrade's book published in 1930 under the title 'The Mechanics of Nature', which has gone through several editions. The text is now about twice as long as the original and considers all the advances of the past thirty years.

The work is presented as a series of 'talks'—one might even call them intellectual conducted tours—on the various branches of physics, which rapidly survey all the landmarks in physics from the origins of modern science up to the present. Possessing a deep knowledge of his subject and combining the experience of a physicist of great distinction with a very wide general culture, Professor Andrade has interspersed his account, which is not without touches of humour, with penetrating and thought-provoking observations, with interesting comparisons, and with informative quotations from other writers of authority. It is surprising to learn, for example, that Newton, with prophetic intuition, had foreseen the danger to humanity of the discovery of means of transmuting the elements.

The scheme of the work unfolds methodically, the order being both logical and chronological. After having reviewed the role of physics and the precise significance to be attributed to its discoveries and theories, Professor Andrade deals in turn with heat and energy, sound and vibrations, light and radiation, electricity and charged particles, solids and liquids, quantum theory, the structure of the atom, the structure of the nucleus, applications of nuclear energy, and lastly with Heisenberg's uncertainties.

The reader is thus gently led by a firm and skilful hand towards the more abstruse branches of physics, finally reaching the extraordinary discoveries of contemporary science. He will be impressed by the clarity and originality of the exposition, by the ease with which the author introduces him to the most difficult problems, and by the talent which he displays in revealing hidden relationships. We found particularly interesting the chapter he devotes to solids and liquids, a subject which he knows most intimately and to which he has made many noteworthy personal contributions, as well as the two chapters dealing with nuclei and applications of nuclear energy.

Recalling that ethical principles possess a permanence never shared by the concepts of physicists, he wisely stresses that it would be vain to base definitive philosophical doctrines on the always provisional results of science.

Professor Andrade's book is a fine work, which presents us with a splendid panorama of the brilliant progress of modern physics and bears witness to the balance and clarity of his thought, based on a wide fund of experience and knowledge. LOUIS DE BROGLIE

ANALYSIS OF DEFORMATION

Analysis of Deformation, *by K. Swainger. Vol. III,* Fluidity. *Pp. xxvii* + 266. *Chapman and Hall Limited, London.* 1956. 65*s. net.*

This volume treats deformation from the viewpoint of fluidity. It is used to provide a platform for the author's critical views on the classical approach and for the presentation of a new theory of fluid motion. The chief feature of this theory is the rejection of the non-linear convective acceleration term in the Euler form of the motion stress equation.

After an introductory chapter there follows an exposition of the mathematical formulation of both the author's theory and the classical theory. The remainder of the book, apart from some unnecessary mathematical appendices, is concerned with applications to topics such as viscous flow and stress-fluidity.

Most of the remarks made in the review of Volumes I and II of the author's series under the present title are still valid and hardly need reiterating, but it is worth noting that on this

occasion as much as seven pages are required to record the 'principal notation'. This is an indication of the difficulty of comprehending the many equations which appear so profusely throughout the book. The author states that 'it was tempting to go on expanding the work . . .' and hints at a second edition. It would perhaps have been better to have delayed writing this book, and the earlier volumes, until the subject matter had settled down into a more stable and acceptable state.

L. S. GODDARD

MAGNETOHYDRODYNAMICS

Magnetohydrodynamics, *by T. G. Cowling. Pp. viii + 115. Interscience Publishers Inc., New York; Interscience Publishers Limited, London.* 1957. *Hard covers,* $3.50*; paper covers,* $1.75 *net.*

The average graduate in physics usually knows a little about the problem of the origin of the Earth's magnetic field, and he may have read something concerning the dynamo theory which is used to explain its maintenance. It is, however, rather unlikely that he will have appreciated that this theory is but one example of the many applications of magnetohydrodynamics, the study of the motion of electrically conducting fluids in the presence of magnetic fields. But if he will turn to this excellent little book he will be rewarded by a glimpse of many fascinating applications of it to problems of sunspot equilibrium, solar streamers and filaments, stellar rotation, magnetic variable stars and ionized gases, and an account of the author's own attempts to explain the darkness of sunspots by magnetic inhibition of convection. He will read of experiments on moving mercury and liquid sodium and perhaps consider that here is a relatively new branch of science which well deserves further study.

L. F. BATES

PHYSICS OF THE SOLID STATE

Introduction to Solid State Physics (*second edition*), *by Charles Kittel. Pp. xvii + 617. John Wiley and Sons Inc., New York; Chapman and Hall Limited, London.* 1956. 96*s. net.*

'To see a World in a Grain of Sand . . .' Solid-state physics has a feast for every scientific taste. The natural historian may collect growth patterns on crystals. The 'Sceptical Chymist' has leave to doubt whether Brillouin zones really explain complex alloy phases with 57 atoms per unit cell. For those who love computing, there are enough sums in the calculation of energy bands to fill all the MANIACS, WHIRLWINDS, and such mathematical toys in the world. Mathematical elegance may flirt with the Ising model and lattice spectra. Superconductivity is a challenge to the most powerful intellects of theoretical physics. Ingenuity may play with tin whiskers and dislocation network.

Ever since its publication, only three years ago, 'Kittel' has been (especially in the United States) the principal entry visa into this land of riches. The new edition has been enlarged in size by about one-half (and in price by rather more). Many sections have been expanded to include new material or to improve the argument. The order of topics has been altered, and several completely new chapters have been added. The work still has the lucidity, the straightforward and brisk style, and the flair for a simple 'physical' explanation, that graced the original. There are a few points of detail open to dispute, and there are some signs of haste in arranging the text and correcting the proofs; but these are minor blemishes in a thoroughly useful book, indispensable for learning, for teaching, and for recalling what every solid-state physicist knows.

J. M. ZIMAN

FIBRE PHYSICS

The Mechanical Properties of Textile Fibres, *edited by R. Meredith. Pp. xii + 333. North-Holland Publishing Company, Amsterdam.* 1956. 61*s. net.*

During the past few years the subject of fibre physics has grown in scope and importance and is attracting the attention of an increasing number of fibre scientists. This monograph forms one of a series covering the rheology of deformation and flow in natural and synthetic substances, and Dr Meredith and his co-authors are to be congratulated on a most serviceable and worthwhile undertaking. This is the first book of its kind to set out to interpret in some detail the mechanical properties of fibres in relation to what is known about their structure.

The subject is developed from basic principles for the three main groups of textile fibres: cellulose, proteins, and synthetic fibres. After dealing briefly with the structure of these groups, the authors trace and relate the structural features with such important aspects of fibres as relaxation and creep, stress-strain relationships, strength, dynamic and mechanical properties, and resilience. The treatment is not encumbered with unnecessary detail. All who are interested in the field of fibre physics will find this book very useful.

R. HILL

TRANSPORT PROCESSES IN CHEMICAL MANUFACTURE

Transport Processes in Applied Chemistry, *by R. C. L. Bosworth. Pp. x + 387. Sir Isaac Pitman and Sons Limited, London.* 1956. 84*s. net.*

This is the third book by the author to deal with aspects of physics which are of fundamental importance in many of the operations of industrial chemistry.

His second book, published in 1952, reviewed recent developments in heat transfer and dealt with this as a transport process basically similar to the diffusion of matter, momentum, and electric charges. The present volume extends this treatment, dealing with a wider range of processes and carrying them further, even to including complete industrial operations. The author deals with the significance and mechanism of processes of transport by molecular motion, and with radiant and convective transfer. There are chapters on turbulent and inter-phase transport, irreversibility, feedback, cascade operations, and chemical similarity. Methods of measuring the efficiency of transport processes are formulated, and a final chapter on the wider aspects of transport processes includes considerations of the driving force and ultimate cost of industrial operations and the efficiency of utilization of energy.

Each chapter is a useful, if necessarily short, review of its particular subject. This, coupled with the unified mathematical treatment of a very wide range of transport processes, should make this book of great value to applied chemists and chemical engineers in universities and industry who wish to gain a deeper, more basic insight into these aspects of industrial operations than is obtained by the classical approach of unit operations.

C. M. NICHOLLS

COLORIMETRIC ANALYSIS

Metallurgical Analysis by means of the Spekker Photoelectric Absorptiometer, *by F. W. Haywood and A. A. R. Wood. Pp. viii + 292. Hilger and Watts Limited, London.* 1956. 40*s. net.*

First published in 1944, this book on colorimetric analysis has been completely revised and brought up to date by A. A. R. Wood in the light of the many recent advances in this field. The writer was associated with the design

and development of the Spekker apparatus and is author of several papers on methods suitable for the analysis of specific elements. The first part of the book deals with the principles of colorimetric analysis, and includes details of the construction, operation, and maintenance of two models of the Spekker photoelectric absorptiometer. In the second part, selected methods of analysis are given for elements usually found in alloys based on aluminium, copper, magnesium, and zinc respectively, and in the more common steels. An extensive bibliography, covering the period 1940–1954, includes original papers on the determination of twenty-two elements by colorimetric analysis using the Spekker absorptiometer. An appendix contains some useful information and includes tables giving the average compositions of various metals and alloys which form suitable chemical standards for this type of analytical work. As a handbook it should be indispensable in all laboratories using the Spekker apparatus. B. W. MOTT

COMPLEX METAL HYDRIDES

Reduction with Complex Metal Hydrides, *by N. G. Gaylord. Pp. xvi* + 1046. *Interscience Publishers Inc., New York; Interscience Publishers Limited, London.* 1956. $15 *net.*

The reduction of organic compounds with lithium aluminium hydride was first described just over ten years ago. Organic chemists were quick to realize the significance of this reagent, which could be used, for instance, to reduce an ester to an alcohol in cold ether. During the past decade the uses of lithium aluminium hydride and related compounds such as sodium borohydride have been manifold, and there has been a growing need for a comprehensive monograph about them. The need is now satisfied by this book, which covers, up to January 1953, in a complete and often critical manner, the preparation and reactions of the complex metal hydrides, including the less common ones such as magnesium aluminium hydride and lithium gallium hydride.

The author deals systematically with the individual hydrides and their reactions with inorganic reagents and with the various groups of organic compounds, concluding with chapters on the experimental handling of the hydrides. No reference will be found to the more recent developments of hydride chemistry, but even so the book will be a necessity for organic chemical laboratories. Its price is unfortunately such that very few chemists will be able to afford a personal copy.

T. G. HALSALL

ACRIDINES

Acridines, *by R. M. Acheson. Pp. xii* + 409. *Interscience Publishers Inc., New York; Interscience Publishers Limited, London.* 1956. $12.50 *net.*

This is the ninth volume of the Interscience series of monographs on 'The Chemistry of Heterocyclic Compounds', and a single reading suggests that it is a praiseworthy book. The material is well arranged in nine chapters dealing with the main group of acridine derivatives, and including chapters on the acridine alkaloids, the absorption spectra of acridines (by L. E. Orgel), and biologically active acridines.

Comparison with Professor Adrien Albert's monograph published in 1951 is inevitable. The two books are differently arranged and completely different in their approach to the subject. The earlier volume contained experimental details of many preparations, and was obviously the work of one who had been long immersed in the subject. Acheson's book is much more the formal monograph, but has the advantage of covering the literature up to 1954.

Acheson devotes seven full pages to the argument about nomenclature and numbering, and reproduces a graph comparing the frequencies with which Graebe's and Richter's numbering systems have been used. Albert used Richter's method, but Acheson, on the basis of his statistical approach, decided on Graebe's system, which is now used by *Chemical Abstracts.*

One may regret the duplication of effort represented by the existence of two works on acridines, but in the outcome it is fortunate that they are both good. K. SCHOFIELD

INDEX OF CRYSTALS

The Barker Index of Crystals, *Vol. II, by M. W. Porter and R. C. Spiller. Pt.* 1, *Pp.* 383*; Pt.* 2, *Pp.* 1800*; Pt.* 3, *Pp.* 1772. *W. Heffer and Sons Limited, Cambridge.* 1956. £10 *net.*

The Barker Index makes it possible to identify a substance by comparison of crystal angles with known values. Over half the measurements available are of monoclinic crystals, and Volume II which deals with these is correspondingly large. To arrange 3572 substances in order of increasing angle *am* between the faces (100) and (110), that is, a 'setting', crystallographic axes, orientation, and indices must be chosen. Since face development controls the setting according to stated rules, varying crystal habit may require alternative settings. This happens for about a third of the first 150 substances.

Apart from possible use for analysis, the volumes form a valuable collection of morphological data. They deal with all monoclinic crystals in Groth's *Chemische Kristallographie*, and some others. The information is authoritative, since, in the course of setting, original investigators' mistakes in calculation, which are numerous and often copied into Groth, have been found and corrected.

Tables of refractive indices, densities, and melting points, with indexes in several forms and references to the index of X-ray data of the American Society for Testing Materials, are valuable added information.

An introduction by M. H. Hey supplements the accounts of Volume I (Part 1) by describing the special applications of the Barker method to the monoclinic system.

An important addition, the lack of which was felt when Volume I appeared, is a single page of brief directions suitable for experienced crystallographers.

The index is reproduced by a photographic method, and the covers are appropriately decorated with a drawing of a Tutton salt. H. M. POWELL

GEOMAGNETISM

Beiträge zur Geschichte der Erkenntnis des Erdmagnetismus, *by H. Balmer. Pp.* 892. *Verlag H. R. Sauerländer & Co., Aarau.* 1956. *Sw. Fcs.* 31.10 net.

This 892-page work is an enlargement of a thesis for a doctorate, the first part giving a general account of the history of geomagnetism from the earliest times to the present day. The second part contains translations of most of the classics of the subject into German, including the letter of Petrus Peregrinus, the whole of Gilbert's *De Magnete*, Stevin's *Havenvinding*, some of Kepler's letters, and much else. This section will be of great value to those whose first language is German, though most of it is already available in English or French. The third section discusses beliefs about two persistent magnetic myths—the existence of an enormous magnetic mountain and the possibility of communicating over

great distances by magnets. There are also 200 pages of brief biographies of about 950 people concerned with the history of geomagnetism, and an account of the development of the subject in Switzerland.

The author rightly calls his work a 'collection' rather than a 'history'; it contains all kinds of interesting things put together without any very profound discussion. The story of the Chinese knowledge of the declination in the twelfth century is, for instance, accepted without a mention of the doubts that most modern commentators have felt about the matter. There is a curious lack of reference to modern works on the history of science—the account of Halley, for example, is largely based on Humboldt's *Kosmos* and does not mention MacPike's books. Silvanus Thompson's translation and commentary on *De Magnete* also are not mentioned. E. C. BULLARD

EFFECTS OF RADIATIONS

Actions chimiques et biologiques des radiations, *edited by M. Haissinsky. Pp. vi* + 221. *Masson et Cie, Paris.* 1956. *Bound, Fcs.* 3400; *paper covers, Fcs.* 2800 *net.*

The second of this series of monographs consists of three contributions. W. Mund gives an account of the chemical effects produced by the passage of ionizing radiations through gases and includes two detailed special sections on inorganic and organic reactions induced by radiation. M. Ageno describes luminescent phenomena produced by high-energy rays and presents recent methods and results in the study of scintillation phenomena. N. Miller's introduction to radiation dosimetry is extremely well set out and should be of great value to workers in many fields. An admirable feature in all the articles, particularly that by M. Ageno, is the close link that is maintained between theory and practice. Of particular importance is the stress laid on the methods used in the various fields, since by this means the reader can appreciate more clearly some of the difficulties of the problems involved and is at the same time provided with useful practical information. The book has an appendix containing conversion factors for physical constants and practical details for radiator dosimetry. One slight criticism is that there is a tendency for the text to invade some of the figures. Otherwise, the monograph is a useful addition to any scientific library.

D. B. ROODYN

BIOCHEMISTRY OF LIPIDS

Biochemical Problems of Lipids (Proceedings of the Second International Conference held at the University of Ghent, 27th to 30th July 1955), *edited by G. Popjak and E. Le Breton. Pp. xvi* + 505. *Butterworths Scientific Publications, London; Interscience Publishers Inc., New York.* 1956. 70*s. net.*

Knowledge of the chemistry and biochemistry of lipids has grown rapidly within the last five years, mainly thanks to the new tools of paper and gas-liquid chromatography and the discovery of coenzyme A and its role in the metabolism of fatty acids. The enzymes responsible for the β-oxidation and for the synthesis of fatty acids have been identified and isolated, and this has led to detailed knowledge of the intermediary metabolism of fatty acids. The biochemistry of phospholipids and of fat transport and the study of nutritional aspects (especially of the unsaturated fatty acids) have also advanced considerably. All these developments and many other aspects are summarized and discussed in the present volume. It contains 69 papers (mostly in English, a few in French or German), together with a brief record of the discussions which followed the presentation of the papers. Many leading workers in the field have contributed, and the result is an authoritative survey of recent and current research on the biochemistry of lipids. H. A. KREBS

ENZYMES AND VIRUSES

Enzyme Antigen and Virus, *by Sir Macfarlane Burnet. Pp. viii* + 193. *Cambridge University Press, London.* 1956. 18*s. net.*

Sir Macfarlane Burnet is well known for his contributions to animal virology, and also for his provocative speculations on wider aspects of biology and medicine.

This book is an extension of the theories put forward in 1949 by Burnet and Fenner in their monograph 'The Production of Antibodies', and is an attempt to link antibody formation with recent knowledge on synthesis of adaptive enzymes and growth of viruses. In all three processes, the cell receives a stimulus which makes it produce a new type of protein. The argument is not always easy to follow, but it eventually leads the author to propose a general information theory based on macromolecular pattern, which he suggests will not be interpreted entirely by the techniques of the physicist and chemist. The work will probably invoke criticism from experts in the various fields which the author covers, but a complacent acceptance of hypotheses based on slender evidence would be the last thing he desires, and it is in any event unlikely in a group of subjects advancing so rapidly. There can be few biologists who have the imagination and breadth of interest of Sir Macfarlane Burnet and could attempt a stimulating work of this kind. M. STOKER

BOTANICAL ATLAS

Botanisk Atlas, *by O. Hagerup and V. Petersson. Pp.* 550. *Ejnar Munksgaard, Copenhagen.* 1956. *Cloth bound, DKr.* 96; *leather, DKr.* 125 net.

This is primarily a collection of drawings of plants which are native, or have been introduced, or have intruded themselves into Denmark. Many of them also occur in the surrounding countries and are common, for example, in southern England. Habit drawings are given of every plant. These are the work of Vagn Petersson and are executed in fine, clear outlines, usually with a minimum of shading. In general, they show the full characters of the plants unambiguously, but grasses, labiates, and others tend to be represented by little more than the inflorescence. The great majority of these drawings were done from living plants, but the potomogetons are from herbarium material. Very numerous enlarged drawings of details are provided by Olaf Hagerup in a style that groups well with the habit drawings. The subjects are chosen to illustrate not only diagnostic characters but also life forms and biological stages. In general they admirably fulfil their purpose, but it is surprising that no indication is given of their magnifications. Some pages are devoted to the general characters of the larger families such as grasses, orchids, and umbelliferae. The book is very elegantly produced on a large page, 11 × 8 in., allowing nearly life-size representation of most of the species. Botanists have much reason to be grateful to the authors.

W. O. JAMES

BOTANY OF TROPICAL CROPS

An Introduction to the Botany of Tropical Crops, *by Leslie S. Cobley. Pp. xv* + 357. *Longmans, Green and Company Limited, London.* 1956. 37*s.* 6*d. net.*

Of a subject as many-sided as the botany of tropical crops, no textbook of convenient size can cover more than

selected aspects. Mr Cobley has chosen to present a wide survey, describing more than 150 species and referring briefly to as many again. Crops are grouped into twelve chapters according to their products—cereals, fibres, oilseeds, and so on. The information given usually includes the systematic position of the plant, its origin and distribution in cultivation, a description of its gross morphology, and notes on uses. Other features of equal importance to the economic botanist, such as population structure and breeding methods, perforce receive scant attention or none.

Within the limits of his choice the author has done a workmanlike job and has been worthily supported by his publishers. The information given is accurate. The 82 plates and 66 figures are judiciously chosen adjuncts to the text. References are given at the end of each chapter for the student who wishes to go deeper.

Designed for students of agriculture, this book should be of particular value to the increasing number receiving training within the tropics.

E. E. CHEESMAN

HUMAN ANATOMY

Textbook of Human Anatomy, *by J. D. Boyd, Sir Wilfrid Le Gros Clark, W. J. Hamilton, J. M. Yoffey, Sir Solly Zuckerman, and the late A. M. Appleton. Pp. xii* + 1022. *Macmillan and Company Limited, London; St Martin's Press, New York.* 1956. £5 *net.*

The conventional undergraduate course in human anatomy is invariably a main target for those who complain about the load of factual knowledge thrust on the unfortunate medical student of today.

This new textbook is an attempt to meet this criticism. In this it has succeeded, in part by omissions—for example, in the section dealing with the locomotor system, where much of the tedious detail of muscular attachments and of classical osteology has been left out—and in part by linking structure to function to produce a more readable and thus a more readily assimilated story—nowhere better illustrated than in Sir Solly Zuckerman's section on the ductless glands. Sir Wilfrid Le Gros Clark gives in the space of only 129 pages an excellent account of the central nervous system and successfully resists the temptation to omit nothing, although some may think that the reticular formation of the brain stem has now qualified for rather more than the two lines allotted to it. Likewise there is a satisfactory and not too prolix account of the main features of the digestive system by Professor W. J. Hamilton which maintains the modern balance between macro- and microscopic anatomy. It seems to be impossible, however, for an anatomist to deal with the peritoneum other than in traditional fashion, deflecting it from here to there, so that the reader begins to feel in the centre of a maze that has no exit. There is no systematic treatment of embryology, but each section gives a brief outline of the relevant development.

The book is profusely illustrated by 796 half-tone drawings, some with colour, X-ray plates, and microphotographs, most of them of a high standard of excellence.

Although the authors claim with justice that they have eliminated much of the detail of classical anatomy, nevertheless this remains a heavyweight textbook, of over 1000 pages. The medical student will undoubtedly find it an interesting and profitable book, to be read and not to be used merely as a reference to supplement dissecting manuals and other short cuts to knowledge.

G. M. WYBURN

THE WORLD OF PLANKTON

The Open Sea: Its Natural History: The World of Plankton, *by Alister C. Hardy. Pp. xv* + 335. *Collins, London.* 1956. 30*s. net.*

Professor Hardy is known to his students as an enthusiast, and perhaps the greatest of his enthusiasms is the world of plankton. As might be expected from the occupant of the Linacre Chair of Zoology and Comparative Anatomy at Oxford University, the enthusiasm is well informed and not, like so much, misdirected. This is not to say that the book is perfect: enthusiasm leads to discursiveness, which, though it helps to hold the reader's interest, makes subsequent reference often difficult. When I first opened this book I felt that accurate photographs or line drawings would form more fitting illustrations than water-colours to a book of this nature, but as I read through and handled it I became a convert to Professor Hardy's mode of illustration. His water-colours do indeed give a far better impression of the living planktonic organisms than any photograph or line drawing could, while accurate detail is supplied by line drawings and the excellent photographs of Dr D. P. Wilson. This general impression, combined with accuracy of detail, make the book an outstanding example of its kind, both for the general reader, for whom it is not too technical, and for the student, or indeed the university teacher.

D. B. CARLISLE

REPTILES

Reptiles, *by Angus d'A. Bellairs. Pp.* 195. *Hutchinson's University Library, London.* 1957. 10*s.* 6*d. net.*

Reptiles living today can be separated into four clearly defined classes: tortoises and turtles, the Tuatara, lizards and snakes, and crocodiles. Extinct forms reveal a far greater diversity of organization, and only by study of them is it possible to obtain a deeper insight into reptile anatomy. The most ancient reptiles appeared in the Carboniferous period. Reptiles flourished throughout the Mesozoic era, which lasted some 120 million years and is also known as the Age of Reptiles. Giant orders of reptiles disappeared towards the end of the Cretaceous period.

It needs considerable courage to produce a comprehensive survey of our knowledge of reptiles within a limited space. The author of this book performed this task with great skill. The reader is first made familiar with the leading anatomical and physiological features of the reptile body. A description then follows of the main classes of fossil and extant reptiles, a final chapter being devoted to the biology of lizards and snakes. The text is relieved by twelve figures and numerous illustrations, and a bibliography of the more important literature provides the interested reader with valuable hints for further study. We owe our thanks to the author for this work and hope that it will enjoy a wide circulation, particularly among students.

E. KUHN-SCHNYDER

PHARMACOLOGY

Medicinal Chemistry, *Vol. III, edited by F. F. Blicke and R. H. Cox. Pp. vi* + 346. *John Wiley and Sons Inc., New York; Chapman and Hall Limited, London.* 1956. 84*s. net.*

This is the third of a series of publications whose object is to provide summaries of the biological properties of substances, particularly for those chemists and pharmacologists most concerned in the elaborating and testing of new drugs. It deals with Methadone

and related analgesics, quaternary ammonium germicides, non-mercurial diuretics, and analogues of physostigmine. The emphasis in these chapters is not so much on the chemistry and physiological action of these compounds as on methods of evaluating their activity and on the correlation of structure and activity. Almost two-thirds of the book is given up to tables relating the structure of compounds with their biological activity. This is the essential feature of the volume, for which reason it should be of value to those actively seeking new therapeutic agents. It should be noted, however, that most of the work which has been sifted and classified was published before 1953.

J. R. P. O'BRIEN

INDUSTRIAL CHEMISTRY

Guida dei principali prodotti chimici, *Vol. I, by Cesare Ferri. Pp. xvi* + 737. *Nicola Zanichelli, Bologna.* 1955. *Lire* 6000 *net.*

The very wide programme suggested by the title is achieved by alphabetical classification according to use. Under petrol additives, lead tetra-ethyl receives special attention, but stabilizers and anti-corrosives are not forgotten. Additives for lubricating oils and auxiliaries in paper and textile manufacture are reviewed, and there is a useful section on motor fuels. Catalysts are set forth in tables and specific ones are named for different processes, polymerization catalysts being discussed separately. There is a concise tabulated account of ceramics. Twenty-eight pages are devoted to a survey of modern dyes. Fuels of all kinds are described. Detergents, explosives, synthetic fibres, photographic chemicals, and pigments occupy the attention of other contributors. No fewer than 159 pages are devoted to pharmaceuticals, two authors sharing the work. The whole subject is well reviewed, and formulae are given for many of the more important antibiotics, vitamins, hormones, and antihistaminics.

Lubricants of all types are considered, and there are valuable summaries of their physical characteristics. Plastics are reviewed by means of a geneological table.

There is unavoidably much variation in the treatment by individual collaborators, but this is preferable to the dull uniformity which might have resulted from a more highly planned effort. Regarded as a whole, this is a valuable work.

E. E. TURNER

CHEMISTRY AND TECHNOLOGY OF WAXES

The Chemistry and Technology of Waxes (*second edition*), *by A. H. Warth. Pp. vii* + 940. *Reinhold Publishing Corporation, New York; Chapman and Hall Limited, London.* 1956. 144*s. net.*

This edition extends to over 900 pages and includes very full descriptive accounts of 'natural' (animal and vegetable) waxes; fossil, lignite and petroleum waxes; and 'synthetic' and compounded waxes of many kinds. There is a prefatory chapter on the chemical components of waxes (which, however, is almost wholly concerned with those of the natural ester-waxes), and two concluding chapters on analytical methods and on the technology of waxes and their uses in industry. The range of materials classified technically as waxes is admittedly very wide and in some ways ill defined; it is therefore all the more desirable that a book of this nature should be composed as explicitly and clearly as possible. Unfortunately the treatment is diffuse in many respects and this detracts from the value of a book which otherwise is a comprehensive and detailed survey of the many substances, natural or artificial, which have waxy properties, irrespective of whether they have so far found industrial applications.

Moreover, instances occur in which reports on waxes are included, both old and recent, with little critical comment on the probable relative accuracy of the sometimes divergent accounts. Thus on page 142 spermaceti is said to melt at 42–46° C and to contain 90 per cent of cetyl palmitate (m.p. 51·6°), whereas the figures on page 147 show that cetyl palmitate cannot amount to more than about one-third of the solid waxes of sperm head oil. Again, it is not sufficiently emphasized that the so-called waxes of Rhus and Myrica berries, and ucuhuba and murumuru 'waxes' (which are seed fats) are wholly glyceridic (fatty) in composition. Similarly, in the chapter on the chemical components of waxes there is some muddled, some probably inaccurate, and not a little superfluous information.

Apart from these defects—all the more unfortunate when dealing with a subject which is in itself both complex and ill defined—the book is a valuable addition to a technological field in which guidance by competent handbooks is still rather inadequate.

T. P. HILDITCH

CONSERVATION OF WORKS OF ART

The Conservation of Antiquities and Works of Art, *by H. J. Plenderleith. Pp. ix* + 373. *Oxford University Press, London.* 1956. 63*s. net.*

This is a book that we have all been awaiting for twenty years. The author's experience of his subject is probably unique, and the book at once becomes the standard textbook and a classic. It is intended for the collector, the archaeologist, the museum curator, and the technician engaged in conservation, and one of the book's most striking features is the completeness with which it caters for the whole range of different attitudes to its very complex subject. A great many people, whatever their interests or discipline, will find it both absorbing and most useful.

The contents impress themselves in two main ways. First, there is the magnificence of the treasures that have passed through the hands of Dr Plenderleith and his associates at the British Museum Laboratory, and the variety and complexity of the problems they present. One feels envious of the opportunity, yet awe of the responsibility—but secure in the knowledge that the objects are in capable hands. Secondly, it is very refreshing to find the most specific sequestering agents jostled by the humble matchstick and spoon.

This kind of work involves electrical, chemical, and mechanical methods, and the best results are obtained by a judicious co-ordination of the three. Almost inevitably it follows that each problem requires highly individual attention. And here a warning: the deceptive ease of the description, and the clarity of the many tables and schemes of treatment, may mask the author's perhaps too quiet insistence on the need for skill and experience.

The book is written with care, taste, and wisdom: it leaves one feeling just the right mixture of respect and unsatisfied curiosity. With it the author firmly stakes his claim for his subject to be considered seriously as a branch of applied science.

L. BIEK

SIR ARTHUR EDDINGTON

The Life of Arthur Stanley Eddington, *by A. Vibert Douglas. Pp. xi* + 207. *Thomas Nelson and Sons Limited, London.* 1956. 25*s. net.*

Arthur Stanley Eddington was essentially a thinker, not a man of action.

It is much more difficult to write the biography of a man whose life has been spent largely in his study than that of a man who has played a prominent part in affairs. Dr Vibert Douglas has succeeded admirably in her account of the life, the scientific work, and the philosophy of a man who was quiet, reserved, and undemonstrative, and who never sought the limelight.

An excellent account is given of the course of Eddington's scientific work on stellar movements, stellar structure, and stellar physics, on relativity, and on fundamental theory. Eddington was the first person in Great Britain to realize the importance and significance of general relativity, and his exposition of the theory did much to secure its acceptance. He was, incidentally, the leader of one of the two British expeditions which in 1919 provided the first verification of the predicted deflection of rays of light in a gravitational field. Eddington combined an appreciation of the problems of observational astronomy with a remarkable physical intuition and great mathematical ability.

By his work on stellar structure, the internal constitution of the stars, and the nature of interstellar matter, Eddington was the pioneer in what has become an important branch of modern astronomy. The meetings of the Royal Astronomical Society, at which these results were expounded, were full of interest and are vividly described.

Eddington exerted a great influence on current thought through his interpretation, by lectures and by writing, of the new ideas that were revolutionizing man's conception of the universe. Miss Douglas gives an excellent account of the development of his philosophical ideas.

Though the book will have its greatest appeal to the physical scientist, all who follow the development of scientific thought will find the book of much interest. H. SPENCER JONES

CHINESE SCIENCE

Science and Civilisation in China, *by Joseph Needham. Vol. II*, History of Scientific Thought. *Pp. xxii* + 696. *Cambridge University Press, London.* 1956. 80*s. net.*

The days of encyclopaedism have gone, but persons still appear with encyclopaedic minds and extraordinary industry, as is shown by the bibliography (pp. 585–683) of this volume, which endeavours to survey Chinese philosophies and discover their influence on the development of Chinese science and technology.

Only recently, however, have specialists with modern training begun working on Chinese philosophies. The first really good history of Chinese thought, that by Feng Yu-lan, appeared only in 1934 and its complete English translation in 1953. Classical Chinese is, moreover, such a concise language that one must first understand a philosophy before translating it! Needham, for example, accepts the following (p. 460) as the translation of the first sentence in a famous Chinese text: 'That which has no Pole! And yet (itself) the Supreme Pole!' I would prefer to translate: 'The Unlimited is the same as the Absolute.' Obviously much work still needs to be done on this philosophy, that of the great Chou Tun-i, before attributing to him a premonition of negative and positive electricity (p. 467).

Against some of Needham's theses there will be strong reaction. Wang Chhung (pp. 368–86) was hardly 'one of the greatest men of his nation in any age' (p. 368). He merely offered a very readable, and partly superstitious, version of the thorough-going naturalism he derived from Hsün Tzu, through his teacher Pan Piao, the father of the great historian. Wang Chhung shows few philosophic originalities, while Hsün Tzu, whom Needham misprizes (pp. 26–29), was one of the dominating influences throughout all of Confucianism. If naturalism promotes science, as Needham assumes, Hsün Tzu was the more scientific.

Although much in this book is inevitably tentative, it contains certain very good discussions. The comparison of the Greek and Chinese ladders of souls (pp. 21–26) is interesting. There is a very good account of Taoism (pp. 33–164), in which there is pointed out both the connection and the lack of connection between this cult and Chinese science. Needham's account of the Later Mohists (pp. 171–84) is excellent. So is his discussion of Tsou Yen (pp. 232–73). Although Needham recognizes that Tsou Yen was not postulating any 'elements' in our sense of the word but rather five 'forces' (p. 244, line 13), he nevertheless still calls them 'elements'. His belief that the modern philosophy of organism is derived, through Leibniz, from Chinese thought (pp. 279–303) is possible, but the relationship appears to me quite unproven. Leibniz was a thinker who required no Chinese stimulus for original ideas. Needham's best worked out section is his discussion of natural law (pp. 518–83).

This book is a highly praiseworthy attempt at a synthesis for which the necessary spadework is as yet mostly not done. HOMER H. DUBS

HISTORY OF IRON AND STEEL

Réaumur's Memoirs on Steel and Iron, *translated by Anneliese Grünhaldt Sisco. Pp. xxxiv* + 396. *The University of Chicago Press, Chicago. Cambridge University Press, London.* 1956. 45*s. net.*

The translation of Réaumur's famous essays on iron and steel of 1722 is of particular value, since no English translation of the complete memoirs existed prior to the present publication. The translation is preceded by an introduction, in which Professor C. S. Smith discusses the significance of Réaumur's work and the background of metallurgical science against which he wrote. R. A. F. de Réaumur (1683–1757), commonly known today by his thermometric scale, was interested in all branches of pure and applied science. His interest in iron and steel began about 1716. It bore fruit in the present treatise of 1722 and a few more metallurgical memoirs read before the French Academy in the following four years, after which he published nothing more on metals. In this short period he made very important contributions to industrial technology. His ideas concerning iron and steel, made known in his memoirs of 1722, 'amounted to prescience', representing a remarkable anticipation of modern knowledge, as Professor R. F. Mehl ('A Brief History of the Science of Metals', pages 5–6, New York, 1948) worded it. In his discussions of the grain size of cemented steel Réaumur anticipated many of the modern American studies of austenite grain size. One of Réaumur's principal inventions, a method of making malleable cast iron, may have been a reinvention of an earlier process patented in 1671 and invented by the ingenious Prince Ruprecht von der Pfalz, who through his mother was a grandson of James I of England. The Prince's and Réaumur's inventions both fell into oblivion, but were resurrected in England shortly after 1800.

H. R. SCHUBERT

Short notices of books

(These notices are descriptive rather than critical and are designed to give a general indication of the nature and scope of the books.)

Recent Advances in Science: Physics and Applied Mathematics, *edited by M. H. Shamos and G. M. Murphy. Pp. xi + 384. New York University Press, New York; Interscience Publishers, New York and London.* 1956. $7.50 *net.*

This is a collection of reports by twelve distinguished American scientists on recent developments in their own fields of physics and applied mathematics. It is a product of the First Symposium on Recent Advances in Science, held at New York University early in 1954. Although it is assumed that the reader has had some general scientific training, no specialized knowledge of the subjects discussed is assumed.

Electrochemistry: Principles and Applications, *by E. C. Potter. Pp. xii + 418. Cleaver-Hume Press Ltd., London.* 1956. 50*s. net.*

This is a comprehensive textbook, with the emphasis laid on principles and their relationship to general applications, designed for both the student and the electrochemical specialist. A knowledge of mathematics and chemistry at roughly the level of the first university year is assumed. There are numerical examples to demonstrate some of the theoretical concepts, and a short bibliography.

Automation: its Purpose and Future, *by Magnus Pyke. Pp.* 191. *Hutchinson's Scientific and Technical Publications, London.* 1956. 16*s. net.*

Opinions vary widely about the speed and extent with which automation will be introduced into industry, but there is no doubt that it is a development that will have far-reaching consequences. This book is principally for the general reader, and sets out both to describe what has already been achieved by means of automation and what can reasonably be expected of it in the fairly near future. There is some discussion of the social consequences of automation, which are certain to play an important part in determining the nature of its application.

The Geographer as Scientist, *by S. W. Wooldridge. Pp. xii + 299. Thomas Nelson and Sons Ltd., London.* 1956. 35*s. net.*

This is a collection of some sixteen lectures and papers prepared by Professor S. W. Wooldridge during twenty-five years of active teaching and research. The selection has been carefully made in order to illustrate the author's views on fundamental questions relating to the scope and nature of geography.

The Friendly Fungi, *by C. L. Duddington. Pp.* 188. *Faber and Faber, London.* 1957. 21*s. net.*

This book, written principally for the general reader, represents a new approach to the problem of the eelworm, one of the most serious of agricultural pests. It describes certain easily cultivated fungi that attack eelworms, and the attempts that have been made to use these fungi to attack the pest in the field.

Fibres, Plastics and Rubbers, *by W. J. Roff. Pp. xvi + 400. Butterworths Scientific Publications, London; Academic Press Inc., New York.* 1956. 63*s. net.*

This is a well-documented reference book intended for those engaged in industrial research and development. It lists, in a form suitable for ready reference, a very great deal of information on the chemical, physical, and general properties of all the most common high polymers, both natural and synthetic. It concludes with a short history of polymers.

Records and Research in Engineering and Industrial Science (*third edition, rewritten and enlarged*), *by J. Edwin Holmstrom. Pp. xii + 491. Chapman and Hall Ltd., London.* 1956. 60*s. net.*

The vast and rapidly growing extent of technological literature makes it increasingly difficult to find information that has already been recorded. This book, by the officer of UNESCO responsible for questions of scientific documentation and terminology, is a detailed guide to the sources and recording of all kinds of technical information.

Vapour Phase Chromatography, *edited by D. H. Destry and C. L. A. Harbourn. Pp. xv + 436. Butterworths Scientific Publications, London; Academic Press Inc., New York.* 1957. 70*s. net.*

The book contains the papers given at a symposium on gas chromatography organized by the Institute of Petroleum in May 1956. It includes the discussion and the recommendations made about nomenclature.

Nouveau traité de chimie minérale, *edited by Paul Pascal. Vol.* x: Azote-phosphore. *Pp. xxxix + 963. Masson et Cie, Paris.* 1956. *Paper covers; Fcs* 6600; *bound: Fcs* 7500 *net.*

This is volume x—although only one other volume has so far been published—of what will ultimately be a very comprehensive nineteen-volume work on inorganic chemistry compiled under the distinguished editorship of Professor Paul Pascal. About two-thirds of the present volume is devoted to nitrogen—by Professor Pascal himself—and the remainder to phosphorus, by Professor René Dubrisay. As was indicated by the form of volume I, the treatment is exhaustive; there is a mass of data and a most extensive bibliography. It is clear that when complete this work will become one of the standard works of chemical reference.

Biographical Memoirs of Fellows of the Royal Society, Vol. II. *Pp.* 345. *The Royal Society, London.* 1956. 30*s. net.*

This is the second of the new series of obituary notices of Fellows of the Royal Society. Following the pattern of the previous volume, it gives authoritative biographies of twenty-two Fellows who died in 1955–56. Each biography gives not only much personal detail and a critical appraisal of the subject's scientific work, but a list of all his publications.

Theories of the Universe, *edited by M. K. Munitz. Pp. x + 437. The Free Press, Glencoe, Illinois.* 1957. $6.50 *net.*

The editor of this book seeks to present a history of cosmology, for the general reader, by means of a selection from the non-technical writings of those who have played a leading part in the development of the subject. Chronologically the span is very great, ranging from Aristotle, Plato, and other philosophers of classical antiquity to Einstein, Hubble, and other cosmologists still living.

Notes on contributors

H. A. KREBS,
M.A., M.D., F.R.S.,

Was born in 1900 at Hildesheim, Germany, and studied medicine at the Universities of Göttingen, Freiburg, Munich, and Berlin. He later worked under Professor Otto Warburg in Berlin and under Professor S. J. Thannhauser at the Medical Clinic at Freiburg. In 1933 he came to Britain as a refugee and joined Sir Frederick Gowland Hopkins' school of biochemistry at Cambridge. From 1935 until 1954 he worked at the University of Sheffield, first as Lecturer in Pharmacology, later as Lecturer and Professor of Biochemistry. In 1953 he was a joint recipient of the Nobel prize for medicine. Since 1954 he has been Whitley Professor of Biochemistry at the University of Oxford. His work has been mainly concerned with the biochemistry of metabolism.

D. McKIE,
Ph.D., D.Sc.,

Was born in Monmouthshire in 1896. He entered University College, London, in 1920 and graduated in chemistry. Now Reader in the History of Science in the University of London. Has written extensively on the history of chemistry, including an authoritative book on Lavoisier's life and work.

M. W. H. BISHOP,
M.A., Ph.D., Dip. Agric. Sci.,

Was born in 1923 and was educated at the Cambridgeshire High School and St Catharine's College, Cambridge. He spent three years with the Iron and Steel Institute and the British Iron and Steel Research Association studying the fouling and corrosion of ships' hulls. In 1947 he returned to Cambridge and in 1949 joined the Agricultural Research Council's Unit of Animal Reproduction in Cambridge, where he first became interested in the physiology of mammalian spermatozoa and fertilization. During 1952–53 he spent a year's leave of absence at the University of Illinois, and in 1955 joined the staff of the Division of Experimental Biology of the National Institute for Medical Research.

C. R. AUSTIN,
D.Sc., B.V.Sc.,

Was born in 1914 in Sydney, Australia, and was educated at Eastbourne College, England, and Sydney University. He was a member of the research staff of the Commonwealth Scientific and Industrial Research Organisation, Australia, from 1938 to 1954, investigating biochemical aspects of pregnancy toxaemia in sheep, the development of special operational and emergency rations for troops, and the physiology of reproduction. He joined the research staff of the Medical Research Council, England, in 1954. He is currently engaged in research on mammalian fertilization and associated phenomena. He has been a Secretary of the Society for Endocrinology since 1956.

L. F. BATES,
B.Sc., Ph.D., D.Sc., F.R.S.,

Was born at Kingswood, Bristol, in 1897, and was educated at the Merchant Venturer's School and the University of Bristol. He served as a commissioned radiographer in India during the first world war, returning to carry out research at Bristol in 1920–22 and in the Cavendish Laboratory, Cambridge, 1922–24. In the latter year he joined the staff of University College, London, and was made Reader in Physics in 1930. In 1936 he was appointed Lancashire-Spencer Professor of Physics at Nottingham, where he has been Deputy Vice-Chancellor of the University. His research school at Nottingham is distinguished for its contributions to experimental magnetism. He was President of the Association of University Teachers 1938–39 and President of the Physical Society 1950–52. His book 'Modern Magnetism' and his British Council publication on 'Sir Alfred Ewing' are well known.

P. W. BRIAN,
Ph.D., Sc.D.,

Was born in Birmingham in 1910 and was educated at King Edward's School, Birmingham, and King's College, Cambridge. He worked at Long Ashton Research Station from 1934 until 1936, when he joined Imperial Chemical Industries Limited as a mycologist at Jealott's Hill Research Station. Since 1946 he has been Head of the Department of Microbiology at the Akers Research Laboratories. He has written numerous papers on the biological activity of fungal metabolic products.

JOHN FREDERICK GROVE,
B.Sc.,

Was born at Sheffield in 1921. Studied at King's College, University of London, under A. J. Allmand. In 1941 he joined Imperial Chemical Industries Limited as a research chemist and was appointed Head of the Organic Chemistry Department of the Akers Research Laboratories in 1950. His publications are concerned mainly with chemicals for pest control, mould-product chemistry, and the application of physical methods to the study of problems in structural organic chemistry.

Some books received

(*Note.* Mention of a book on this page does not preclude subsequent review.)

AGRICULTURE

Chemicals, Humus and the Soil, *by Donald P. Hopkins. Pp.* 288. *Faber and Faber Ltd., London.* 1957. 25*s. net.*

Yearbook of Forest Products Statistics, 1956. *Pp. vi* + 170. *Her Majesty's Stationery Office, London.* 1957. 12*s.* 6*d. net.*

BIOCHEMISTRY

Carotene: Its Determination in Biological Materials, *by V. H. Booth. Pp. vii* + 119. *W. Heffer & Sons Ltd., Cambridge.* 1957. 18*s. net.*

Venoms, *edited by Eleanor E. Buckley and Nandor Porges. Pp. xii* + 467. *American Association for the Advancement of Science, Washington, D.C.; Bailey Bros. and Swinfen Ltd., London.* 1956. 86*s. net.*

BIOLOGY

Genetic Studies with Bacteria, *by M. Demerec, Z. Hartman, P. E. Hartman, T. Yura, J. S. Gots, H. Ozeki, and S. W. Glover. Pp. v* + 136. *Carnegie Institution of Washington, Washington D.C.* 1956. *Paper bound,* $0.80; *cloth bound,* $1 *net.*

Man as an Animal, *by W. C. Osman Hill. Pp.* 176. *Hutchinson University Library, London.* 1957. 10*s.* 6*d. net.*

Proceedings of the Third Berkeley Symposium on Mathematical Statistics and Probability. *Vol. IV,* Biology and Problems of Health, *edited by Jerzy Neyman. Pp. viii* + 179. *University of California Press, Berkeley; Cambridge University Press, London.* 1957. 43*s.* 6*d. net.*

BOTANY

How to know Western Australian Wildflowers, *Pt. II, by W. E. Blackall and B. J. Grieve. Pp. xxxiii* + 138 + *xxii. The University of Western Australia Press, Nedlands, Western Australia.* 1957. 30*s. net.*

Anatomie végétale, *Vol. III, by Édouard Boureau. Pp. viii* + 227. *Presses Universitaires de France, Paris.* 1957. *Fcs.* 1500 *net.*

CHEMISTRY

Chemistry: The Conquest of Materials, *by K. Hutton. Pp. xi* + 228. *Penguin Books Ltd., Harmondsworth, Middlesex.* 1957. 3*s.* 6*d. net.*

The Chemistry of Vegetable Tannins. A Symposium held at Cambridge University, April 12–13th, 1956. *Pp.* 160. *Society of Leather Trades' Chemists, Croydon.* 1956. 30*s. net.*

Colorimetric Analysis (*second edition*). *Vol.* 1, Determinations of Clinical and Biochemical Significance, *by N. L. Allport and J. W. Keyser. Pp. xi* + 424. *Chapman and Hall Ltd., London.* 1957. 50*s. net.*

Organic Syntheses, *Vol.* 36, *edited by N. J. Leonard. Pp. vi* + 120. *John Wiley and Sons Inc., New York; Chapman and Hall Ltd., London.* 1956. 30*s.* net.

Quelques problèmes de chimie minérale. 10*th Chemistry Council held at the University of Brussels,* 22–26 *May,* 1956. *Pp.* 544. *Published for the Institut International de Chimie Solvay by R. Stoops, Brussels.* 1956. *Paper covers, Belg. fcs.* 590; *bound, Belg. fcs.* 675 *net.*

Technique of Organic Chemistry, *Vol. III. Pt.* 1. Separation and Purification, *edited by Arnold Weissberger. Pp. ix* + 873. *Interscience Publishers Inc., New York; Interscience Publishers Ltd., London.* 1956. $17.50 *net.*

ENGINEERING

The Analysis of Engineering Structures (*third edition*), *by A. J. S. Pippard and J. F. Baker. Pp. xii* + 564. *Edward Arnold (Publishers) Ltd., London.* 1957. 60*s. net.*

Atomic Energy in Canada, *by C. C. Kennedy. Pp.* 96. *Atomic Energy of Canada Ltd., Ontario.* 1956. $1 *net.*

GENERAL SCIENCE

Selected Scientific Papers from the Istituto Superiore di Sanità, *Vol. I, Pt.* 1. *Pp.* 233. *Fondazione Emanuele Paternò, Rome.* 1956. 57*s.* 6*d. net.*

Space Research and Exploration, *edited by D. R. Bates. Pp.* 224. *Eyre and Spottiswoode, London.* 1957. 25*s. net.*

MEDICINE

Documenta Ophthalmologica, *Vol. X. Pp.* 382. *Uitgeverij Dr W. Junk, The Hague.* 1956. 92 *guilders.*

MINERALOGY

Clays and Clay Minerals. Proceedings of the Fourth National Conference on Clays and Clay Minerals, *edited by Ada Swineford. Pp. vii* + 444. *National Academy of Sciences—National Research Council, Washington, D.C.* 1956. $6 *net.*

PHYSICS

American Institute of Physics Handbook, *edited by Dwight E. Gray. Pp. ix* + 1524. *McGraw-Hill Book Company Inc., New York; McGraw-Hill Publishing Co. Ltd., London.* 1957. £5 12*s.* 6*d. net.*

Basic Foundations of Isotope Technique for Technicians, *edited by W. C. Smullen. Pp. xx* + 163. *Charles C. Thomas, Springfield, Illinois; Blackwell Scientific Publications, Oxford.* 1956. 36*s. net.*

Causality and Chance in Modern Physics, *by David Bohm. Pp. xi* + 170. *Routledge and Kegan Paul Ltd., London.* 1957. 21*s. net.*

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